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TROPICAL DISEASES BULLETIN

VOL. 35.] 1938. [No. 5.

IMPERIAL MYCOLOGICAL INSTITUTE 21 MAY 1938

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Issued under
the Direction of the
Honorary Managing Committee of the
BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street, London, W.C.1.

Price 2/6 Net.] *Entered as Second Class Matter in the U.S.A. Post.* [Annual Subscription 21/-. With Supplement 25/-.

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 35.] 1938. [No. 5.

TRYPANOSOMIASIS.

Jacono (I.). Ulteriore contributo alla proposta di una nuova classifica dei tripanosomi. [**Further Contribution to the Proposed New Classification of the Trypanosomes.**]—*Ann. di Med. Nav. e Colon.* 1937. May–June. 43rd Year. Vol. 1. No. 5–6. pp. 237–8, 241–2. With 14 figs. (2 coloured) on 3 plates.

The author, considering the peculiar large trypanosomes which occur in the blood of frogs, proposes to limit the genus *Trypanosoma*, Gruby 1843, to these and similar forms and to place all other trypanosomes of the more conventional type in the genus *Castellanella*, a name which was proposed for certain forms by Chalmers in 1918. This division fails to recognize the fact that the peculiar forms in the frog are really abnormal overgrowth forms which have remained over from an ordinary type of infection in the tadpole. *C. M. Wenyon.*

Castellani (A.) & Jacono (I.). Ricerche sulla biologia della *Castellanella gambiensis* in vitro. [**Biology of *Trypanosoma gambiense* in vitro.**]—*Riv. di Parassit.* Rome. 1937. July. Vol. 1. No. 3. pp. 181–193. With 1 fig. English summary (3 lines).

—— & ——. Osservazioni su un caso di malattia del sonno. [**Observations on a Case of Sleeping Sickness.**]—*Ibid.* pp. 195–210. With 16 figs. English summary (3 lines).

—— & ——. Ricerche sperimentali sul polimorfismo della *Castellanella gambiensis*. [**Polymorphism of *Trypanosoma gambiense*.**]—*Ibid.* pp. 211–220. With 22 figs. (3 coloured). [12 refs.] English summary (3 lines).

These papers, three in number, are based on a fatal case of sleeping sickness which occurred in an Italian who returned to Rome after residence in the Congo. They appear to contain little that is new and, judging from the verbatim repetition in all three papers in this one number of the journal of a section including a diagram devoted to the classification of trypanosomes, a section which is again reproduced twice in other papers from the same institute (*v.* Guidetti and Castellani & Jacono below), they might be judged to have been written largely for the purpose of bringing forward the unusual and incorrect name for *Trypanosoma gambiense* which appears in the titles.

Some of the figures in the coloured plates appear to the reviewer to depict organisms which resemble flagellates from contaminated distilled water rather than trypanosomes. *C. M. W.*

GUIDETTI (Carlo). Ulteriore contributo alla conoscenza della morfologia delle *Castellanelle brucei*. [**Further Contribution to our Knowledge of the Morphology of** *Trypanosoma brucei*.]—*Giorn. Ital. di Clin. Trop.* 1937. Aug. 31. Vol. 1. N.S. No. 8. pp. 227–8, 231–4. With 8 figs.

By exposing *Trypanosoma brucei* (referred in the paper to the genus Castellanelle or Castellanella) from the blood of guineapigs suffering from what the author terms castellanosis to the action of certain dyes *in vitro*, various involution forms, described as being crithidia-like, leptomonas-like, or plasmodium-like, are produced. It is concluded that the dyes stimulate the production of those forms which occur during the course of development of the trypanosome (castellanelle) in the intermediate host. The account of the new classification of trypanosomes with its accompanying diagram, which has been published in four other papers, is again produced here. *C. M. W.*

CASTELLANI (A.) & JACONO (I.). Tentativi di immunità attiva nelle infezioni sperimentali da *Castellanella gambiensis*. [**Attempts at Active Immunization in Experimental** *Trypanosoma gambiense* **Infection.**]—*Policlinico.* Sez. Med. 1937. July 1. Vol. 44. No. 7. pp. 325–335. With 1 fig.

The authors have made various attempts to immunize guineapigs against the trypanosome of sleeping sickness (styled *Castellanella gambiensis*). They find that it is possible to increase the natural resistance of the guineapig by the use of an antigen consisting of blood rich in trypanosomes ("ricco in castellanelle") treated with small quantities of bile or defibrinated homologous blood rich in the dead bodies and products of autolysis of trypanosomes ("castellanelle"). It is perhaps worth noting further that in this paper there is produced for the fifth time the section and figure devoted to the classification of the trypanosome of sleeping sickness, which has been the subject of comment above. *C. M. W.*

BOURGUIGNON (G. C.). Notes épidémiologiques sur la trypanosomiase humaine dans le Sud-Est du Congo Belge. [**Epidemiological Notes on Sleeping Sickness in the South-East of the Belgian Congo.**]—*Bull. Méd. du Katanga.* 1937. Mar. Vol. 14. No. 1. pp. 1, 3–9, 11–19, 21–9, 31–6. [24 refs.]

The observations recorded in this paper were made in the course of two journeys to the Province of Elisabethville during 1935 and 1936. The author confines himself to parasitological considerations bearing on the epidemiology of sleeping sickness in that area. The first journey was made to the Lualaba and Tanganyika districts between 18th August and 21st October, 1935, and the main object was to collect for VAN HOOF strains of trypanosomes from cases of sleeping sickness. In all, 24 such strains were obtained by direct inoculation of blood from 29 cases of sleeping sickness into guineapigs. Details are given

in a table. As a rule, the guineapigs exhibited an intense infection, the blood often showing 100–200 trypanosomes per microscope field after about 40 days ; the majority of the animals died within 3 months. The infection in Cercopithecus was less intense and less fatal. This work suggests that, in general, the strains from Lualaba and Tanganyika are particularly virulent for guineapigs. The author considers the question of mechanical transmission and reaches the conclusion that this is a danger which is far from negligible.

In certain regions *G. palpalis*, *G. morsitans*, *G. pallidipes* and *G. longipalpis* were all found. One patient at Bukama was infected with a parasite which, according to VAN HOOF, had the characters of *T. rhodesiense*. This strain in the guineapig was resistant to a dose of 1 gm. per kilo. of tryparsamide and was cyclically transmissible by *G. palpalis*. Other strains obtained during this journey exhibited marked differences from the Leopoldville or Mayumba strains examined by VAN HOOF in 1933. After considerable discussion, the author concludes that the factor most likely to explain this exaltation of virulence of the trypanosome is the presence in the region in question of different species of Glossina able to transmit *T. gambiense*.

There follow certain remarks on arsenic-resistance. This was apparently not manifest clinically, but several of the strains sent in guineapigs to VAN HOOF exhibited an increased resistance to tryparsamide. *W. Yorke.*

NORTHERN RHODESIA, GOVT. OF : VETERINARY DEPARTMENT. ANNUAL REPORT FOR THE YEAR 1936 [MORRIS (J. P. A.), Director of Veterinary Services]. Appendix C. pp. 64–65.—**Trypanosomiasis** [LE ROUX (P. L.), Veterinary Research Officer].

The dairymen in the mining area in the north have continued to experience great direct and indirect losses from tsetse fly disease. It is stated that "Some have found 'Antimosan' an excellent prophylactic." [It would be interesting to know exactly what this means.]

Because Surfen C was very favourably reported from Kenya and Nigeria, it was tested out here, but with disastrous results. Some of the animals tolerated the drug fairly well, but others died within 15 minutes with froth and blood running from the nostrils. Post-mortem examination revealed extensive haemorrhages throughout the lungs.

The agitation of the Abercorn planters induced the Government to approach the Tanganyika Government for a loan of the services of Mr. Swynnerton and Mr. Burtt. These officers submitted reports and made recommendations, which have since been put into practice. Morris writes that the recommendations are sound, but he doubts whether much would be achieved unless some attempt is made at reducing the food supply of *G. morsitans*. The few buffalo in the valley could probably be shot out. The Mpulungu area appears an ideal spot for investigating the eradication of *G. morsitans* by means of limiting the food supply.

During the author's recent visit to the Abercorn area he tried to ascertain whether there were occasions of fly encroachment, but the information received was rather vague. He believes that in some localities the fly has definitely receded. The large tracts of land owned by the British South Africa Company are no longer inhabited by

natives, and increase of game has resulted since the removal of the natives into reserves. This is undesirable, as the game may act as vectors in the dissemination of rinderpest and similar diseases.

W. Y.

Gold Coast Colony. Report on the Department of Animal Health for the Year 1936–37 [Stewart (J. L.), Director of Vet. Services]. [**Trypanosomiasis** pp. 15–21.]

It has been found that *T. simiae* occurs in pigs in the forest and causes great and sudden mortality. A Syrian owner in Ashanti lost 150 pigs in a few weeks from this type of trypanosomiasis. Trypanosomes swarm in the blood and the pathological effect appears to be an acute septicaemia. The usual porcine trypanosomiasis is that caused by *T. brucei*, which appears to have a predilection for pigs. Another interesting discovery was a number of cases where *T. theileri* were found in large numbers in the blood of cattle.

Therapeutic experiments with "Surfen C" were not successful with cattle, but good results were claimed in canine trypanosomiasis. Over 50 laboratory cattle were treated by this drug and there were few cures and many relapses. The most effective drug is still tartar emetic. In *T. brucei* infections of horses and pigs nagonal was used, but in horses this drug caused swellings under the abdomen, ulcerated anus and a high temperature for about 4 days; the treatment, however, cured the 5 horses to which the drug was given.

A lengthy account is given of tsetse fly eradication work in the Pong-Tamale and other areas. *W. Y.*

i. van Hoof (L.), Henrard (C.) & Peel (E.). Sur le rôle du porc indigène comme réservoir de *Trypanosoma gambiense*. [**The Native Pig as a Reservoir of** *T. gambiense*.]—*C. R. Soc. Biol.* 1937. Vol. 126. No. 24. pp. 72–75.

ii. ——, —— & ——. Rôle du porc comme réservoir de *Trypanosoma gambiense*. [**The Pig as a Reservoir of** *Trypanosoma gambiense*.] —*Ibid.* pp. 1245–1248.

i. After referring briefly to the inconclusive results of the earlier attempts to infect pigs with *T. gambiense*, the authors describe their own experiments. The pigs used were born and bred in Leopoldville, far from any focus of Glossina. Notwithstanding the improbability of a natural infection with *T. brucei*, numerous blood examinations were made to exclude this. Four such pigs were infected with *T. gambiense*—two by blood inoculation and two by the bite of infected tsetse. All became infected, and from each Glossina were infected. In later experiments two laboratory-bred young pigs were used and these likewise were readily infected by the bites of infective tsetse.

The general conclusion reached is that the native pig is an ideal reservoir of *T. gambiense*. The parasite is scanty in the blood, it does not produce the slightest pathological reaction, and it readily infects Glossina. The pig may remain, for at least a year, an active reservoir of *T. gambiense*; and the parasite may acquire in it a complete resistance to tryparsamide, and morphological characters—numerous short forms and posterior nuclear forms—resembling those of *T. brucei* or *T. rhodesiense*.

ii. Here the authors continue their work to prove that the pig is a reservoir of *T. gambiense*. Glossina were fed on a patient infected with a tryparsamide sensitive strain of *T. gambiense*. The strain was then passed by cyclical transmission through a series of three pigs, and flies infected from the third pig were then fed on a human volunteer and on a fourth pig and two guineapigs. The fact that the man became infected shows that the pig can act as a reservoir of *T. gambiense* pathogenic to man. *W. Y.*

Curasson (G.). Les trypanosomiases virulentes du porc en Afrique. Observations personnelles sur celle à *T. brucei* en Afrique Occidentale française. [**Virulent Trypanosomiasis of the Pig in Africa. Personal Observations on that due to *T. brucei* in French West Africa.**]—*Rec. Méd. Vét. Exot.* 1937. July–Sept. Vol. 10. No. 3. pp. 109–119. With 2 figs. [14 refs.]

After summarizing previous work on porcine trypanosomiasis, Curasson passes to an account of his own observations. He states that he has seen numerous cases of natural infection of pigs, especially in 1929 and 1934. In 1929 he encountered a very fatal epidemic in the region of Bamako. Of 800 animals more than 500 died of a chronic form of the disease with little in the way of signs beyond progressive emaciation. The blood contained a trypanosome indistinguishable from *T. brucei*—a diagnosis which was confirmed by Mesnil.

In 1934, there was another epidemic, also in the vicinity of Bamako. When the author had to deal with it only 8 of 50 animals survived. In 4 days the 8 survivors had also perished. This infection was, in contrast to the former, extremely virulent, killing the pigs in 2 to 4 days. Trypanosomes in the blood were numerous and the parasite had the same morphological characters as that causing the 1929 epidemic; it was diagnosed as *T. brucei*. The trypanosome was subinoculated into the dog, sheep, rabbit, guineapig, rat, *Cricetomys gambianus*, *Grossarchus obscurus* and *Procavia* sp. In all it produced a rapidly fatal disease.

T. brucei infections in the pig may therefore be benign or severe. The cause of this variability is discussed and, in the author's opinion, the increase in virulence may be due to successive reinfections and numerous passages through the pig. Possibly other factors like avitaminosis may also play an important part. The paper concludes with a brief discussion of the nomenclature of the pig trypanosomes and the conclusion reached is that they belong to two types, *congolense* and *brucei*. *W. Y.*

Hoare (C. A.). **On the Nomenclature of the Trypanosome causing Acute Porcine Trypanosomiasis in Africa.**—*Bull. Soc. Path. Exot.* 1937. Oct. 13. Vol. 30. No. 8. pp. 686–692. [18 refs.]

This paper is devoted to a discussion of the correct name of the trypanosome causing acute porcine trypanosomiasis in Africa. The issue lies between the names *T. suis* Ochmann, 1905, *T. simiae* Bruce *et al.*, 1912, and *T. porci* Schwetz, 1932.

The history and status of these names are considered in chronological order, and the conclusion is reached that the correct and only valid name for the polymorphic trypanosome causing acute trypanosomiasis in African pigs is *T. simiae* Bruce *et al*, 1912. This name has

priority over *T. porci* Schwetz, 1932, in accordance with Article 27 of the International Code of Zoological Nomenclature. The name *T. suis* is not valid, as it does not comply with the requirements set down in Article 25. The synonymy of the trypanosome is as follows :—

T. simiae Bruce *et al.*, 1912.
Synonyms : *T. ignotum* Kinghorn *et* Yorke, 1912.
Duttonella simiae (Chalmers, 1918).
T. rodhaini Walravens, 1924.
T. porci Schwetz, 1932.
T. congolense porci Schwetz, 1934.
? [*T. suis* Ochmann, 1905].

W. Y.

Slatineanu (A.), Balmus (G.) & Balmus (P.). Sur une épizootie due au trypanosome Lewisi-Kent. [**An Epidemic due to** *T. lewisi*.] —*Arch. Roumaines Path. Expérim. et Microbiol.* Paris. 1937. June. Vol. 10. No. 2. pp. 159–170. With 6 coloured figs. on plates. [16 refs.]

A severe epidemic arose spontaneously amongst the authors' stock rats during last winter. The multiplication of rats suddenly stopped, and most of the young rats failed to increase in weight. The animals suddenly lost their activity. Some of them became somnolent and stopped feeding ; they had diarrhoea, the coat was staring, there was no fever, but pronounced dyspnoea.

After about a week or ten days a second phase of the disease set in. This was characterized by a blepharo-conjunctivitis, and sometimes by a haemorrhagic lesion at the tip of the nose, which often became gangrenous. The animal became very dyspnoeic, emaciated and cold. The feet were pale, oedematous and often exhibited small haemorrhages. Many of the animals died.

Investigations show that this epidemic was due to *T. lewisi*. The general conclusion is drawn that, under certain conditions unfavourable to the rat, this trypanosome can produce severe and fatal epidemics.

W. Y.

Nash (T. A. M.). **Advice on Tsetse Surveys and Clearings.** Revised Edition. 1937. July. 9 pp. Kaduna : Govt. Printer.

In his introduction the author states that this revised edition of his pamphlet has become necessary in order to embrace the results of recent research and a more extensive knowledge of conditions in the Northern Provinces of Nigeria. The object of the paper is to simplify the subject by making generalizations that will be universally applicable ; but this is not easy in a country the size of Nigeria with a vegetation ranging from mangrove swamp to desert scrub. Nash hopes, however, that the general principles laid down will prove helpful as a working basis.

The paper is written in simple language for the benefit of the layman. A brief description is given of the general appearances of the commonest Nigerian species, *viz. G. morsitans*, *G. tachinoides* and *G. palpalis* ; this is followed by some remarks on a tsetse survey and by an account of the haunts of the three species.

Nash then passes to the subject of clearings. He points out that these are of two kinds, *viz.* aggressive and defensive. A tsetse survey

in the late dry season often shows that tsetse, which have been menacing settlements during the rains, are dependent for their existence upon a distant dry season concentration area. The removal of this fly sanctuary may stop the wet season spread into the settlements, but such aggressive clearing should not be attempted by the layman as it requires expert judgment.

Defensive clearing aims at protecting the population from attack by tsetse during the course of their normal work, or whilst travelling along the trade routes; it aims at reducing man-fly contact to negligible proportions by removing the riverine vegetation which enables tsetse to penetrate the areas frequented by man; no attempt is made to exterminate the fly; it is merely driven back to a safe distance. The matter is discussed in respect of each of the three species of tsetse mentioned above, and the paper ends with some notes on the correct method of clearing riverine vegetation. *W. Y.*

Stewart (J. L.). **Eradication of Tsetse-Flies of the *G. palpalis* Group from the Pong-Tamale Area, Northern Territories, Gold Coast.** No. 1 of 1937. 18 pp. With 1 map. [13 refs.] 1937. Accra: Govt. Printer & London: Crown Agents for the Colonies, 4 Millbank, S.W.1. [1s.].

This article must be consulted in the original by those interested. It contains a description of a successful aggressive anti-tsetse clearing scheme to eliminate fly from a defined area. The flora and methods of clearing are fully described, and the bionomics of the *G. palpalis* group are discussed. *W. Y.*

Corson (J. F.). **A Second Note on the Infectivity to Man of a Strain of *Trypanosoma rhodesiense*: Resistance of Two African Volunteers to Infection.**—*Jl. Trop. Med. & Hyg.* 1937. Nov. 1. Vol. 40. No. 21. pp. 263–266.

In previous papers the results are given of experiments which were made on man with a strain of *T. rhodesiense* which had been maintained for a considerable period in sheep and antelopes [this *Bulletin*, 1937, Vol. 34, p. 931].

The present paper describes further experiments on four African volunteers in connexion with the transmission of this strain through two more antelopes, *viz.* an impala and a bushbuck, in succession.

The author gives the following summary of his experiments :—

" Two experiments were made, in each of which a single *G. morsitans*, infected with *T. rhodesiense*, failed to produce infection in one volunteer and afterwards infected another.

" The infections produced by the bites of these flies in control animals gave no indication that the general virulence of the strain of *T. rhodesiense* had become less during maintenance for nearly three years in ruminant animals and *G. morsitans*.

" The infections in white rats, which were bitten by these two flies before and after the dates on which the volunteers were bitten, were similar, and indicated no change in the virulence of the trypanosomes in either of the flies during their infective life. It seems to be clear, therefore, that volunteers Masungwi and Bundala were more resistant than the other two, and this suggests that in nature many persons are bitten by infective flies without becoming infected. If that is so it seems also to be probable that cases of inapparent infection, such as that described by Lamborn

and Howatt (1936), may not be of rare occurrence, and that some infected people may recover spontaneously. It was shown long ago, in experiments with *T. brucei* and *T. gambiense*, that even such susceptible animals as white rats, guinea-pigs, and monkeys may resist infection, and sometimes spontaneous recovery occurs. In experiments with single *G. morsitans*, infected with *T. rhodesiense*, I have not yet found that any of the ordinary susceptible laboratory animals has failed to become infected after being bitten, nor has there been any case of spontaneous recovery among them but, as virulence is relative to the animal, it is very probable, by analogy with *T. brucei* and *T. gambiense*, and with the recovery of antelopes from infection with *T. rhodesiense*, that in man also spontaneous recovery may take place. It would be interesting if similar experiments with a suitable strain of trypanosomes were made on volunteers in Europe to see whether, like African natives, some are resistant. In such experiments I think that the question of inapparent infections has to be considered; Duke (loc. cit.) recorded the case of a volunteer whose blood showed no trypanosomes until the fifty-first day after his first inoculation of infected blood and the eighteenth day after the second, yet his blood was infective to a monkey twenty days after his first inoculation. It is possible also that the action of Bayer 205 on the kidneys should be considered, as it varies in different persons, but the drug has now been used in thousands of cases and the action on the kidneys seems to be temporary only."

W. Y.

REICHENOW (Eduard). Dauerkultur pathogener Trypanosomen. [**The Culture of Pathogenic Trypanosomes.**]—Reprinted from *C. R. XIIe Congrès Internat. Zool. Lisbonne 1935.* pp. 1955-1968. [13 refs.]

The work recorded in this paper has already been published elsewhere and noticed in this *Bulletin* [*vide* 1930, Vol. 27, p. 244, and 1935, Vol. 32, p. 34]. *W. Y.*

VAN HOOF (L.), HENRARD (C.) & PEEL (E.). Influence de repas préliminaires indifférents sur l'évolution de *Trypanosoma cazalboui* chez *Glossina palpalis*. [**Influence of a Preliminary Uninfected Meal on the Evolution of** *Trypanosoma cazalboui* **in** *Glossina palpalis*.]—*C. R. Soc. Biol.* 1937. Vol. 126. No. 34. pp. 1249–1252.

In a previous paper [this *Bulletin*, 1937, Vol. 34, p. 926] the authors have shown that a preliminary meal on normal animals decreases the infectibility of *G. palpalis* when it is subsequently fed on an animal infected with *T. gambiense*. This trypanosome undergoes a long and complicated evolution in the body of the insect. At first it multiplies actively in the lumen of the intestine, but it seems that it can usually escape the expulsive force of the digestive flux if it is able to invade the extraperitrophic space.

It may be that several normal meals taken before the infected feed may cause chemical changes preventing the flagellates obtaining a foothold in the extraperitrophic space, or possibly the first meal made by a tsetse coincides with the final development of the peritrophic membrane and with the filling of the extraperitrophic space by digestive fluid. If this be the case it would seem that the tsetse is more likely to become infected if its first meal is on infected blood.

The evolution of *T. vivax* in Glossina is not so complicated, and the present paper is concerned with ascertaining whether preliminary meals on normal blood have any influence on the capacity of tsetse to become infected with this trypanosome if subequently fed on infected animals.

The experiments show that preliminary meals on normal blood did not modify the infectibility of *G. palpalis* with *T. vivax*. Comparing these results with those obtained with *T. gambiense*, the authors see an argument against the hypothesis that *T. gambiense* at once installs itself within the salivary passages of *G. palpalis* [*vide* the hypothesis of SCHILLING *this Bulletin*, 1937, Vol. 34, p. 125]. *W. Y.*

VAN HOOF (L.), HENRARD (C.) & PEEL (E.). Action de repas médicamenteux sur l'évolution des trypanosomes pathogènes chez la "Glossina palpalis." [**The Effect of a Drug Meal in the Evolution of Pathogenic Trypanosomes in** *G. palpalis*.]—*Ann. Soc. Belge de Méd. Trop.* 1937. Sept. 30. Vol. 17. No. 3. pp. 385–440. [19 refs.]

The authors inquire whether the presence of a drug in the blood ingested by a tsetse can destroy the trypanosomes in the fly, or whether such a meal has any action on the trypanosomes at any stage of their development in the fly. Many investigators have attempted to solve these problems and a brief summary of their results is given.

The present experiments are divided into two groups, *viz.*, those performed with tryparsamide and those in which Bayer 205 was used. Attempts were first made to disinfect isolated infective Glossina by feeding them on guineapigs a few hours after they had been given a dose of tryparsamide. The next set of experiments was devised with the object of ascertaining whether a preliminary feed on tryparsamide blood had any action on the development of *T. gambiense* in the tsetse; in this work the flies were fed on a guineapig which had, a few hours previously, been given a dose of tryparsamide, and then on an infecting animal. The number of flies which became infected was compared with the number becoming infected in control experiments in which the flies were given a preliminary meal on a normal guineapig instead of on one which had had tryparsamide. In the third set of experiments a meal of tryparsamide blood was given, whilst the trypanosomes were developing in the tsetse fly in order to ascertain whether the drug exerted any influence on the evolution of the parasites in the fly. In each of the three sets of experiments observations were made on normal and arsenic-resistant strains of *T. gambiense*.

The experiments in which Bayer 205 was used were of a similar nature, except that only normal strains of *T. gambiense* were used. The paper concludes with a record of similar experiments with trypanosomes pathogenic to domestic stock, *viz. T. brucei*, *T. congolense* and *T. cazalboui*.

The general conclusions of this interesting and painstaking work are as follows:—

1. A meal on blood containing tryparsamide or Bayer 205 does not destroy *T. gambiense* infecting the intestine, proventriculus and salivary glands of Glossina. Even the salivary gland trypanosomes found in the proboscis of infective Glossina do not appear to be affected. A limited experiment suggests that the same is true for neosalvarsan and the antimonial Sdt. 411 Bayer.

2. Nevertheless, an important proportion of tsetse thus treated, although they harbour trypanosomes in the salivary glands and appear to be infective, are no longer able to transmit the infection to guineapigs.

3. The prolongation of the incubation period in guineapigs, bitten by tsetse treated in this manner, confirms the view that the drug had changed the virulence of the trypanosomes, even though it had failed to produce morphological changes.

4. The preliminary meal on tryparsamide or Germanin blood did not influence the evolution of *T. gambiense* in the tsetse, unless the drug was present in very large amounts. Such preliminary meals of drug containing blood did not cause the trypanosomes to become drug-resistant.

5. A preliminary feed on tryparsamide blood had no inhibitory effect on the development of tryparsamide resistant trypanosomes in the testse, even though the dose of the drug given to the guineapig was appropriately large in relation to the degree of resistance of the trypanosome.

6. The disinfecting meals given to tsetse during the course of the developmental cycle of the trypanosomes gave results similar to those given with isolated infective flies. They did not lessen the frequency of the infections, but they inhibited or delayed transmission of the infection to guineapigs.

Analogous results were obtained with *T. brucei*. *T. congolense* appeared to escape entirely the action of a drug meal. *T. cazalboui*, however, responded definitely to the influence of a Germanin meal, which decreased notably the frequence of infections. *W. Y.*

VAN HOOF (L.), HENRARD (C.) & PEEL (E.). L'infection proventriculaire permetelle de pronostiquer à coup sur l'invasion ultérieure des glandes salivaires de " Glossina palpalis " par " Trypanosoma gambiense " ? [**Does Proventricular Infection imply Ultimate Invasion of the Salivary Glands of** *G. palpalis* **by** *T. gambiense* ?]—*Ann. Soc. Belge de Méd. Trop.* 1937. Sept. 30. Vol. 17. No. 3. pp. 441–459. With 1 chart. [12 refs.]

This paper deals with a subject which has recently been fully discussed by MURGATROYD and YORKE in an article which had apparently not come to the notice of van Hoof and his colleagues [this *Bulletin*, 1937, Vol. 34, p. 533]. After referring to the differences of opinion between TAYLOR (1932) and DUKE (1933) on the subject of the significance of proventricular invasion, they quote the reviewer (1936), who stated that he had found that proventricular infection did not necessarily imply subsequent gland infection ; and that he believed loss of transmissibility occurred in three stages, *viz.*—firstly, the trypanosome lost the capacity to pass from the proventriculus to the salivary glands ; then it lost the capacity to spread forwards in the extraperitrophic space to the proventriculus ; and, lastly, it lost the capacity of establishing itself in the extraperitrophic space. In the present paper van Hoof and his colleagues bring forward certain facts which support this view.

It is difficult to do justice to this paper in a summary of moderate length and it should be consulted in the original by those interested. The authors deal with three strains of *T. gambiense*, the first was non-transmissible, the second feebly transmissible, and the third easily transmissible by *G. palpalis*. Full details are given in a series of tables of the results of dissection of the flies which were fed on each of these strains and which survived more than a few days after the infective meal. Of the 1,428 flies fed on the non-transmissible strain, dissection

showed 40 intestinal and 8 proventricular infections; among the 1,380 flies fed on the feebly transmissible strain there were 20 intestinal, 31 proventricular and 3 gland infections; and among the 245 flies fed on the easily transmissible strain there were 30 intestine, 10 proventricular and 7 gland infections.

The authors reach the general conclusion that proventricular infection does not necessarily imply ultimate invasion of the salivary glands, and does not give any certain indication of the cyclical transmissibility of a strain. It marks, however, a particular stage in the developmental cycle of the trypanosome, because it allows of the recognition of special long thin forms, which apparently are destined to invade the salivary glands.

The infection of the proventriculus by these special forms confirms the belief that the normal infection of Glossina by *T. gambiense* is by the indirect route and dependent upon a preliminary development in the intestine [*vide* this *Bulletin*, 1937, Vol. 34, p. 125]. *W. Y.*

Lewis (E. Aneurin). **Tsetse-Flies in the Ol Orokuti Area of the Masai Reserve, Kenya Colony.**—*Bull. Entom. Res.* 1937. Oct. Vol. 28. Pt. 3. pp. 395–402. With 1 fig. (map). [12 refs.]

A description is given of the fly belts in the Ol Orokuti area of the Masai Reserve. The paper seems to be of local interest and must be consulted in the original by those interested. *W. Y.*

Bax (S. Napier). **The Senses of Smell and Sight in** *Glossina swynnertoni*. —*Bull. Entom. Res.* 1937. Dec. Vol. 28. Pt. 4. pp. 539–582. With 18 figs. & 2 plates.

Glossina swynnertoni is attracted by the scent of oxen up to about 180 feet, and by sight of moving oxen up to 450 feet.

In the experiments on scent perception, tsetse flies were placed in a cage (77 × 22 × 26 inches) covered with mosquito netting standing about two feet from the ground, in an enclosure of grass screens, while a team of six oxen with two men was driven past the enclosure at varying distances up wind. The movements of the flies were observed during the passage of the oxen and in control periods before and after. Increased activity, indicating perception of the scent, was observed at ranges of 110–180 feet for male flies, but failed at 300 ft. Female flies reacted only up to 110 ft.; wind was blowing at 1½ to 5½ miles per hour in these experiments. There was no response to shouting or the trampling of oxen, or to scent of manure, hessian, etc., though the exhaust of a lorry at 300 ft. was attractive to the flies.

In the experiments on vision, a gap was cut in the circumference of the enclosure and the oxen were passed by to leeward. The maximum degree of contrast was ensured by using black oxen against a light background in bright sunshine. Positive results (increased activity on the part of the flies) were obtained up to a range of 450 ft. with male flies; there was no reaction at 600 ft. The responses were diminished when the contrast was less, as when the sun was obscured or the background in semi-shadow. A small dark screen at 110 ft. gave as good reactions as the span of oxen.

These observations bear out the conclusion that both sight and scent are important in the behaviour of tsetse flies ; the relative importance of these senses doubtless differs from one species to another.

V. B. Wigglesworth.

JACK (Rupert W.) & WILLIAMS (W. L.). **The Effect of Temperature on the Reaction of *Glossina morsitans* Westw. to Light. A Preliminary Note.**—*Bull. Entom. Res.* 1937. Oct. Vol. 28. Pt. 3. pp. 499–503. With 3 figs.

In the course of recent work certain facts of considerable interest concerning the phototropic reactions of *Glossina morsitans* have been established. The reaction to light of active flies of this species at normal indoor temperatures is positive. MELLANBY (1936) had also found the same in respect of *G. palpalis*.

In their present experiments, the authors have shown that if the temperature is raised sufficiently, the reaction of the flies is reversed and becomes strongly negative.

The apparatus used in these experiments is described in detail. It consists essentially of an insulated cage divided by a removable partition into two approximately equal sections. The top and end of one section are glazed and the other walls painted white. The second compartment is dark, and the walls blackened. The source of light used in the tests was a 100-watt electric bulb above the glass roof of the light compartment, a water screen being interposed to intercept the heat rays.

The flies showed no negative reaction to this light at temperatures below 30°C., but by raising the temperature to the requisite height in the light section, every fly could be driven into the dark section, where it would remain. A fly which has once exhibited the negative reaction will usually return promptly to the dark section if driven out, provided that the temperature does not fall. The negative reaction occurred whether the temperature in the dark section was below, equal to, or above that of the light section. It was even found that flies would leave an uncomfortably high, but not immediately fatal, temperature in the light section (42°C.) for a rapidly fatal temperature in the dark section (49°C.), dropping dead very shortly after entering the latter. The reaction is therefore definitely negative to light itself, and is independent of the relative temperature in the light and dark.

The negative reaction to light is also exhibited at high temperatures by *Stomoxys calcitrans*, but not so strongly as by tsetse. The common Rhodesian house-fly, *Musca vicina*, displays a far greater ability to find a more comfortable temperature by the process of trial and error independently of the light conditions, although, even in this species, strong light may assist the search.

Under natural conditions the temperature in the shade is, of course, always lower than in the sun, and the reaction described above is obviously the guiding impulse by which the fly is rapidly translated, when necessary, from the dangerous heat of the sun's rays to the cooler refuge of the shade.

The authors discuss this reaction in relation to the movements of *G. morsitans* in the forest, in the interior of dense patches of evergreen forest, along river banks and during the heat of the day in the savannah forest. They reach the conclusion that the distribution of tsetse flies

in relation to the vegetation and other features of their habitat at any given time may be explicable to a large extent on the basis of phototropic reactions. *W. Y.*

Corson (J. F.). **The Use of Isolated Infective Flies in Transmission Experiments with** *Glossina morsitans* **and** *Trypanosoma rhodesiense.* —*Jl. Trop. Med. & Hyg.* 1937. Oct. 15. Vol. 40. No. 20. pp. 248–249.

This article, which must be consulted in the original by those interested, states the various disadvantages resulting from the use of boxes of flies in experiments on the transmission of trypanosomes by Glossina. In Corson's opinion, much is to be said for employing isolated flies in work of this sort. *W. Y.*

Tanganyika Territory. Annual Medical and Sanitary Report Year ended 31st December 1936 [Scott (R. R.), Director of Med. Services]. [**Trypanosomiasis** p. 114].

A native child of about fourteen years of age was admitted to hospital suffering from ascites and enlarged glands in the neck. *T. rhodesiense* was found in the blood. Appropriate treatment was given, but the child died from intercurrent disease two months later.

An unusual feature of the case was the discovery of enormous numbers of trypanosomes in the ascitic fluid. A single drop of the fluid was found to swarm with them. The fluid contained large numbers of cells of the lymphoid or mononuclear type. Large mulberry cells were also found, which the author believed to resemble the " morular " cells of Mott. *W. Y.*

Menk (W.) & Bock (E.). Zur Klinik und Behandlung der afrikanischen Schlafkrankheit. Kurzer Bericht ueber 4 Fälle. [**The Clinical History and Treatment of Four Cases of African Trypanosomiasis.**] —*Arch. f. Schiffs- u. Trop.-Hyg.* 1937. Dec. Vol. 41. No. 12. pp. 751–754.

These four cases are recorded because they indicate the necessity of most careful examination for evidence of trypanosomiasis in patients returning from sleeping sickness areas, even though they may not exhibit any of the classical signs of disease.

One of the patients, who at first had symptoms suggestive of a latent infection with trypanosomes, was found also to be suffering from diabetes mellitus, filariasis, tertian malaria and ankylostomiasis. It is interesting to note that control of the diabetes by insulin was in no way interfered with by intensive germanin and atebrin treatment. The treatment of the trypanosomiasis by germanin appeared to provoke the latent tertian malaria.

The *Microfilaria diurna* in the blood were uninfluenced by germanin and atebrin. The complications in no way interfered with the action of germanin on the trypanosome infection. *W. Y.*

Orlovitch. Sur les résultats de l'action préventive du Bayer 205 ou moranyl dans une région à forte endémie de maladie du sommeil. [**The Prophylactic Action of Bayer 205, or Moranyl, in a Heavily Endemic Sleeping Sickness Region.**]—*Ann. Soc. Belge de Méd. Trop.* 1937. Sept. 30. Vol. 17. No. 3. pp. 353–359. With 1 graph.

This paper describes a large scale experiment to ascertain the prophylactic value of moranyl. The district chosen was a limited region, bounded on the east by the Boma-Lukula railway and on the west by the Lukunga river, which is a tributary of the Congo ; the total population comprised 621 persons. In this district the disease has always maintained the upper hand in spite of all efforts to master it. Families were to be found consisting of 10–15 individuals, not a single one of whom had escaped the disease. A certain equilibrium appeared to have been reached prior to 1934, when the number of cases seemed to increase, and at the end of that year 20 new cases (7·6 per cent. of the population) were found, but probably the actual number of cases was double this. In view of this the control measures were tightened up, but a census in August 1935 showed 15 new cases for the first 7 months of the year. As in November 1935, seven new cases were discovered, it was decided to moranylize all those who had enlarged glands whether positive or negative. These, which numbered 75, were treated as follows :—

29 adults each received 3 gm. of moranyl in a week.
40 children received 1 to 1·25 gm. in a week.
6 infants received 0·45 to 0·60 gm. in a week.

No accident attended this dosage, except that some cases exhibited transient albuminuria which disappeared in 8 days.

As, however, a further examination of the population in January 1936 revealed 7 new cases, it was decided to moranylize the entire population, consisting of 160 men, 260 women, and 201 children. After having made 86 gland punctures with 7 positive results, 93 blood centrifugalizations with 1 positive result, and 32 thick blood film examinations, moranylization was commenced as follows :—

Adults received 1 gm of moranyl intravenously.
Children received 0·4 to 0·75 gm. of moranyl intravenously.
Infants received 0·15 to 0·3 gm. intramuscularly.

The only untoward results were occasional febrile disturbances with rigors and headaches lasting up to 2 hours.

Three months later 44 gland punctures were made, and 72 blood centrifugalizations and 29 thick blood films were examined without a single positive result. The moranylization was then repeated. After still another 3 months the population was again examined with negative results and a third dose of moranyl given. The last examination, made 3 months after the third dose of the drug, has failed to reveal a single case of the infection amongst those treated, but 4 natives, who for one reason or another were not treated, had become infected. *W. Y.*

Murgatroyd (Frederick). **Observations on the Therapeutic Action of Three Arsenicals, Neocryl, K. 324 and K. 352, in Gambian Sleeping Sickness.**—*Ann. Trop. Med. & Parasit.* 1937. Dec. 21. Vol. 31. No. 4. pp. 473–542. [12 refs.]

The author has tested the therapeutic value of neocryl [this *Bulletin*, 1936, Vol. 33, p. 659] and of two other arsenicals prepared

for the Chemotherapy Committee of the Medical Research Council, *viz.* K. 324 and K. 352 [this *Bulletin*, 1935, Vol. 32, p. 699], on sleeping sickness cases in the Gambia. In all, 122 cases were treated with neocryl; 44 of these had normal cerebrospinal fluids, and 78 pathological fluids. As a routine, 10 doses of 0·045 gm. per kgm. body weight were given at weekly intervals, but many of the patients attended irregularly, and in a few cases higher doses up to 0·06 gm. per kgm. body weight were given. The results of treating these cases are summarized in tables.

Neocryl produced a rapid and definite clinical improvement in practically every case treated, although some of the patients were in a very advanced stage of the disease. A considerable number of patients felt so well after a few doses that they absconded. Of the early cases with normal spinal fluids 30 finished a course of treatment; all were clinically improved, two experienced visual disturbances from which complete recovery was made, and one relapsed 16 weeks after finishing treatment.

In the cases with pathological spinal fluids, 46 finished a course of treatment, and of these 35 were clinically improved and their spinal fluids changed towards normality. One case failed to improve clinically, and in three others trypanosomes failed to disappear from the spinal fluid, although the general condition was improved. In 4 cases there was clinical improvement and parasites disappeared from the spinal fluid, but neither the protein nor the cell count was improved. Three patients receiving routine doses suffered from toxic effects which were attributed to the drug, one having an attack of vomiting and abdominal pain, and two experiencing transient disturbances of vision, which in one case was very slight. Another patient, after a large dose, had gastro-intestinal symptoms; another had a short attack of dizziness, which could not be definitely associated with the drug, and still another suffered loss of vision, which was probably due to the disease rather than to the drug. Four patients relapsed during the period of observation, which varied from patient to patient, but in some instances was over 4 months.

Murgatroyd writes that these results resemble those which would have been expected from tryparsamide, and probably the two drugs are very similar in their actions. It is, however, impossible to draw any accurate comparison until the later fate of cases treated with neocryl is known. Arrangements have been made with various medical officers in the Gambia to continue the observation of patients where possible.

The clinical tests with K. 324 and K. 352 gave unsatisfactory results. They were found to be toxic for man in relatively small doses, and all doses up to the maximum tolerated were ineffective in the therapy of human cerebral trypanosomiasis. *W. Y.*

Acres (Ian S.). **The Treatment of Sleeping Sickness with Neocryl.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1937. Nov. 30. Vol. 31. No. 3. pp. 333–338.

The author has tested the therapeutic action of neocryl on cases of sleeping sickness at the Baptist Mission Hospital at Bolobo in the Belgian Congo. The following summary is given :—

"1. A series of twenty-one cases of sleeping sickness were treated with neocryl with dosage similar to that of tryponarsyl, the Belgian equivalent of

tryparsamide : three cases previously unresponsive to arsenical compounds were similarly treated.

" 2. In first stage cases there was definite clinical improvement, and the immediate results as determined by gland and lumbar puncture were satisfactory.

" 3. In second stage cases despite marked clinical improvement, the immediate results were not so satisfactory. The result of the treatment in these cases seems uncertain, in view of the rapid relapse of Cases C2 and C4, and the trypanosomes persistent in the blood of Case C6. In reference to this last case it is worthy of note that in the blood of some cases treated with tryponarsyl in our district trypanosomes can be found even after a full course of the drug.

" 4. In cases previously treated by arsenical compounds the results were not encouraging.

" 5. No advantage was found in giving injections twice weekly, although the number of cases treated thus does not perhaps permit a fair comparison.

" 6. No definite toxic reaction was noted, except in cases previously treated with tryponarsyl. A dose of 3 grammes twice weekly was given without untoward effect in a normally developed man.

" 7. It is impossible to compare the result of treatment with neocryl with that of tryponarsyl (tryparsamide) until the cases reported have been followed up for at least 2 years, but the evidence submitted in the addendum suggests that it is definitely inferior to tryponarsyl."

In an addendum, the author states, after his paper was sent for publication, it became evident that there were many relapses. Accordingly, he re-examined all the test cases before six months had elapsed after their courses of treatment. Of 9 first-stage cases, 2 had to be taken under treatment again because of raised cell count in the cerebrospinal fluid. Of 12 second-stage cases, 7 or 8 have relapsed and have been treated again. The author remarks that the 2 first-stage cases which relapsed were those treated by two injections weekly. This is a remarkably high relapse rate and the symptoms in most cases have returned.

Acres considers that on the whole neocryl is apparently a somewhat dangerous drug to use in sleeping sickness, as it gives rather rapid clinical improvement, which, however, is only temporary in second-stage cases. The danger is in the treatment of cases who cannot adequately be followed up and who disappear before the end of treatment. *W. Y.*

Lourie (E. M.) & Yorke (Warrington). **Studies in Chemotherapy. XVI. The Trypanocidal Action of Synthalin.**—*Ann. Trop. Med. & Parasit.* 1937. Oct. 22. Vol. 31. No. 3. pp. 435–445. [47 refs.]

The authors give the following summary of their work :—

" 1. Attention is drawn to the recent interesting observation of the Jancsós and of Schern and Artagaveytia-Allende that synthalin exerts a curative action on mice infected with various pathogenic trypanosomes.

" 2. It is pointed out that the considerations which led these two groups of workers independently to make this discovery were apparently the same, *viz.*, that trypanosomes require for their metabolism a large quantity of sugar, and that synthalin when given in large doses produces a pronounced hypoglycaemia. A summary of the literature bearing on these matters is given.

" 3. Reference is made to the fact that both Jancsó and Schern, as the result of a detailed consideration of the manner in which synthalin exerts its therapeutic action in experimental trypanosomiasis, reach the

conclusion that it is mainly due to the fact that the drug produces a hypoglycaemia; both workers, however, recognize the possibility that a direct action of the drug on the parasite may play a subsidiary rôle in the therapeutic process.

"4. Our experiments on the therapeutic action of synthalin on mice infected with various pathogenic trypanosomes confirm those of Jancsó and of Schern. A single large dose (0·075 mgm. per 20 gm. mouse) produced a definite therapeutic effect on mice infected with *T. equiperdum*, and on mice infected with the normal, the atoxyl-resistant and the Bayer-resistant strains of *T. rhodesiense*. With repeated doses of the drug it was found possible to cure a certain proportion of infected animals.

"5. In order to throw light on the problem whether the therapeutic action of synthalin is due to a direct toxic action on the trypanosomes, or whether it is an indirect effect resulting from a hypoglycaemia, we have examined the trypanocidal action of the drug on suspensions of trypanosomes *in vitro* by means of the technique described in previous papers of this series.

"It was found that synthalin (and synthalin B) exerts *in vitro* a powerfully trypanocidal action which is of the same order as that of the aromatic trivalent arsenicals, a concentration of only 1 : 262,000,000 sufficing to destroy practically all the trypanosomes in the suspensions within 24 hours. It was also found that synthalin is just as active *in vitro* for the atoxyl- and Bayer-resistant strains as for the normal strain.

"The trypanocidal action of insulin *in vitro* is relatively negligible.

"These observations seem to warrant the conclusion that the therapeutic action of synthalin depends upon a direct lethal effect of the drug on the parasite.

"6. This demonstration of the powerfully trypanocidal action of synthalin has encouraged a search for similar or allied compounds of equal trypanocidal activity and of less toxicity for the host. The results obtained with a considerable series of such substances prepared by Dr. H. King will be published in the near future." *W. Y.*

King (H.), Lourie (E. M.) & Yorke (Warrington). **New Trypanocidal Substances.**—*Lancet.* 1937. Dec. 11. pp. 1360–1363.

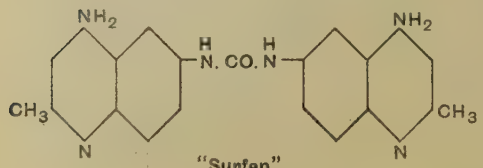
This investigation was prompted by the discovery (*vide* above) that synthalin has a direct trypanocidal action. A considerable number of guanidines, isothioureas, amidines and amines, with alkyl and alkylene chains, were prepared, and their trypanocidal activity *in vitro*, their toxicity for mice, and their therapeutic action on infected mice examined.

It was found that some of these compounds, notably certain members of the diamidines, exhibited a powerful trypanocidal action *in vitro*. With the most active member of the series, undecane 1 : 11 diamidine, it was possible to produce permanent cures in infected laboratory animals. As undecane diamidine is of entirely different chemical constitution from all known trypanocidal substances, the discovery is of considerable academic interest. It is also of practical significance, in that it opens up a new field in the search for substances of therapeutic value against trypanosomal infections. *W. Y.*

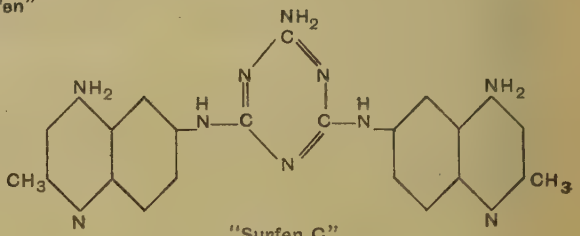
Iensch (H.). Neue Chemotherapeutika der 4-Amino-chinolin-Reihe. [**New Chemotherapeutical Drugs of the 4-Aminoquinoline Series.**] —*Angewandte Chemie.* 1937. Nov. 27. Vol. 50. No. 48. pp. 891–895.

This paper records the results of an unusual method of conducting a chemotherapeutical investigation, *viz.* the development of drugs

from a starting-point, 4-aminoquinoline, selected on purely academic grounds. Out of the large number of derivatives made, two, bis-2-methyl-4-aminoquinolyl-6-carbamide and bis-2-methyl-4-aminoquinolyl-6-melamine, to which the names "Surfen" and "Surfen C" have been given, were considered to be worth clinical trial.



"Surfen"



"Surfen C"

"Surfen" has been recently introduced as a non-staining antiseptic which is claimed to be more active in living tissues than *in vitro*. "Surfen C" has been the subject of a number of references in this *Bulletin* (1935, Vol. 32, p. 686; 1936, Vol. 33, pp. 169, 170, 173, 175; 1937, Vol. 34, pp. 103, 117, 119, 521, 554). *T. congolense* infections in horses and cattle, hitherto almost uninfluenced by drugs, have been treated by it with encouraging results, in the Sudan (Vol. 34, p. 119), Uganda (Vol. 33, p. 175) and Tanganyika (Vol. 33, p. 170), but in Nigeria with less success (Vol. 33, p. 169). In *T. brucei* infections in cattle, which are extremely resistant to treatment, it has given good results (Vol. 33, p. 175). Use of this drug in human trypanosomiasis is contra-indicated by the production of acute nephritis (Vol. 32, p. 686; Vol. 33, p. 169). A third substance related to these two, in which the two amino-methylquinoline nuclei are joined by a diallylmalonyl group, is stated to possess activity against *Trypanosoma cruzi*, which has not been affected hitherto by any chemotherapeutic agent. This has not been given a trivial name. *W. H. Gray.*

Browning (C. H.), Morgan (G. T.), Robb (J. V. M.) & Walls (L. P.). **The Trypanocidal Action of Certain Phenanthridinium Compounds.** —*Jl. Path. & Bact.* 1938. Jan. Vol. 46. No. 1. pp. 203–204.

Two of a series of phenanthridine and phenanthridinium compounds possess curative action in mice experimentally infected with trypanosomes. These are :—

A. 7 amino-9 (p-aminophenyl)-10 methyl phenanthridinium chloride (NH_2 groups at positions 7 and X).
B. 3(acetylamino)-9 (p-acetylaminophenyl)-10 methyl phenanthridinium chloride ($NH.COCH_3$ groups at positions 3 and X).

Both of these compounds in doses approaching the maximum tolerated (one subcutaneous injection of 1 mgm. of A, or 2·5–5·0 mgm.

of B for a mouse of 20 gm.) are curative for mice infected with *T. brucei* when administered 24 hours after inoculation. Compound A has likewise a curative action on *T. congolense* infections in mice, whilst Compound B, which is without effect on this trypanosome, has a marked therapeutic action on *Sp. minus* in mice, although the largest doses do not lead to cure. Both compounds act on a strain of *T. brucei*, which is completely resistant to the largest tolerated doses of arsacetin.

These phenanthridinium compounds constitute a new type of trypanocidal agent. *W. Y.*

STRANGEWAYS (Winifred I.). **The Trypanocidal Activity *in vitro* of Aromatic Thioarsinites and Neo-Arsphenamine.**—*Ann. Trop. Med. & Parasit.* 1937. Oct. 22. Vol. 31. No. 3. pp. 387–404. [17 refs.]

Reference is made to the work of the reviewer and his colleagues which showed that, whereas pentavalent arsonic acids had very little trypanocidal activity *in vitro*, all compounds containing trivalent arsenic, whether arsenoxides, thioarsinites or arseno-compounds were lethal to trypanosomes at very high dilutions.

A series of stable chemical compounds formed by the condensation of aromatic arsenoxides with sulphydryl compounds were prepared by KING. It was found that in nearly all cases these compounds were less toxic to the hosts than their content of arsenoxide would lead one to expect, while in many cases a substance with a high therapeutic index was produced by the condensation with sulphydryl compound of an oxide with a low therapeutic index.

Miss Strangeways considered that an investigation of the trypanocidal activity *in vitro* of compounds of this type might throw some light on the exact form in which they exert their lethal effect. It might be supposed either (1) that they act without chemical change in structure, or (2) that they must first undergo hydrolytic fission with the production of the intensely active arsenoxide.

The methods used for this study were also applied to neoarsphenamine, which also might be supposed to exert its curative action either (1) in the unchanged condition, or (2) after oxidation to the active arsenoxide.

The technique employed was that employed by YORKE, ADAMS and MURGATROYD (1929) and details of the experiments are given in detail.

The conclusions reached are as follows :—

" *Thioarsinites* have a toxicity for trypanosomes *in vitro* in high dilution. That this toxicity is due to the hydrolysis of the compound in aqueous solution with liberation of the highly trypanocidal arsenoxide is shown by :

" 1. The identity in the lethal activity of equimolecular concentrations of thioarsinite and its parent oxide.

" 2. The inhibition of the lethal action both of an arsenoxide and a thioarsinite in strong solution by the addition of 10 molecules excess of glutathione, and the failure to obtain protection in higher dilutions owing to the preponderating influence of water molecules.

" Now, thioarsinites have been shown to be more effective as therapeutic agents in experimental trypanosomiasis than the corresponding arsenoxides (Cohen, King and Strangeways, *Jl. Chem. Soc.*, 1931, p. 3043). Since, as is shown above, the directly trypanocidal agent of a thioarsinite is the arsenoxide, this requires some explanation.

" Thioarsinites are readily obtained in solution as neutral sodium salts. At the relatively high concentrations (1 in 1,000 to 1 in 100) in which these solutions are introduced into the blood-stream, there is very little hydrolysis to the arsenoxide and sulphydryl components, as shown by a negligible nitroprusside reaction. After intravenous injection and consequent dilution of thioarsinite, there will be some hydrolysis with liberation of free arsenoxide. This partial hydrolysis is rapid, since the trypanosomes begin to disappear from the blood-stream within half an hour after injection ; but it is not immediately complete, since, as has been pointed out above, the dose of a thioarsinite which can be tolerated is greater than would be expected from the calculated content of arsenoxide.

" *Neoarsphenamine* has a trypanocidal action *in vitro* in low concentrations, although these are higher than those found for arsenoxides and thioarsinites. This toxicity is not increased by aerial oxidation during the course of an experiment. The addition of 10 molecules excess of glutathione to strong solutions of neoarsphenamine inhibits its lethal action, although a similar excess is without effect on the toxicity of high dilutions. This lends support to the suggestion that neoarsphenamine is adsorbed by the trypanosome and becomes oxidized, within the trypanosome or on its surface, to the highly trypanocidal arsenoxide. The inhibitory action of glutathione would, then, be the same as in the case of arsenoxides and thioarsinites."

W. Y.

STRANGEWAYS (Winifred I.). **Observations on the Trypanocidal Action *in vitro* of Solutions of Glutathione and Ascorbic Acid.**—*Ann. Trop. Med. & Parasit.* 1937. Oct. 22. Vol. 31. No. 3. pp. 405–416. With 1 chart. [11 refs.]

The investigation recorded in this paper was the result of a phenomenon observed in the author's previous work. It was found that different concentrations of glutathione in Tyrode solution containing an equal volume of heated serum, or in Tyrode alone, exerted a definite lethal action on suspensions of trypanosomes. Death of the trypanosomes in such a medium did not occur earliest in the highest or the lowest concentration of glutathione, but in an intermediate zone of concentrations. When, on the other hand, fresh unheated serum was used for the medium, the trypanosomes usually remained healthy in all but the highest concentrations of glutathione.

As a result of her analysis of this phenomenon, Miss Strangeways considers that she has obtained a certain amount of evidence in support of the hypothesis that the formation of hydrogen peroxide during the oxidation of solutions of glutathione and ascorbic acid is responsible for their trypanocidal activity. The exact mechanism of this formation is, however, not apparent. It might be supposed (1) that the hydrogen peroxide is formed by aerial oxidation, either immediately or on standing, of solutions of the two compounds ; or (2) that the oxidation takes place as a result of the metabolic processes of the trypanosomes themselves. These alternative hypotheses are considered at some length.

The author summarizes her work by stating that in neutral or slightly alkaline solutions of glutathione and ascorbic acid exposed to air, a substance is rapidly formed which is very toxic for trypanosomes *in vitro*. Evidence has been produced for the identity of this substance with hydrogen peroxide. *W. Y.*

Radna (R.). Etude sur le problème de la trypanosomiase chimio-résistante. Nouvelle méthode de traitement. [**On the Problem of Drug-Resistance in Trypanosomiasis.**]—*Ann. Soc. Belge de Méd. Trop.* 1937. Sept. 30. Vol. 17. No. 3. pp. 361–374.

Drug-resistance is a very real danger, not only to the patient himself, but also owing to the difficulties which it creates in attempts to deal with a focus of trypanosomiasis. The only way to deal satisfactorily with such a patient is to remove him to a place which is not infested with Glossina. This, however, is not easily done, because certain resistant cases may escape observation and because the patients object to isolation.

After these preliminary observations the author passes to a description of his own investigations. He first decided to examine whether the trypanosomes from an arsenic-resistant case behave differently from those from a normal case when tested *in vitro* against an arsenical drug. Resistant cases are defined as those who were refractory to a course of 15 injections of tryponarsyl followed by emetic or trystibine. The trypanosomes were obtained by triple centrifugation of the patient's blood. A drop of the deposit, rich in trypanosomes, was added to a drop of 1 : 200 tryponarsyl, and the mixture (hanging drop preparations) kept at 37°C. All the parasites—normal and resistant alike—disappeared in an hour. From this the author concludes that the resistant parasites were *in vitro* just as chemo-sensitive as were the normal parasites. [This sort of work is open to very severe criticism. No controls appear to have been used. Would the parasites have lived under the conditions of the experiment in the absence of tryponarsyl? This drug is a most unfortunate one for the purpose in question : it is well known that the pentavalent arsenicals are practically inactive, whereas the trivalent compounds kill the normal trypanosomes when present in only 1 in 100 millions. The reviewer and his colleagues have proved beyond all doubt that resistant strains of trypanosomes exhibit great resistance *in vitro*.]

The next part of the paper deals with agglutinins. The sera of 11 normal untreated cases contained practically no agglutinins, but after treatment they exhibited considerable agglutinating and lytic power. The sera of the resistant cases exerted no agglutinating or lytic action after treatment. From these observations the author conceived the idea of giving his resistant cases a combined treatment consisting of a transfusion of blood from the convalescent normal patients and a dose of tryponarsyl. He claims that whilst neither of these measures alone did any good, the combination of convalescent serum and drug produced sterilization. *W. Y.*

French (M. H.). **Changes in the Sedimentation Rates of the Red Blood Corpuscles during Trypanosome Infections.**—*Jl. Comp. Path. & Therap.* 1937. Sept. Vol. 50. Pt. 3. pp. 191–194.

In the course of nutritional and biochemical studies on trypanosomiasis in the larger farm animals the opportunity was taken of studying the sedimentation rates of the red cells. It was found that there was a big difference in the sedimentation rates of normal healthy cattle and sheep blood when compared with donkey's blood. Increased sedimentation rates follow infection with *T. congolense* and *T. brucei*, but the increase is small in cattle, slightly greater in sheep, and very much more marked in donkey's blood. *W. Y.*

PACKCHANIAN (Ardzroony). **The Electrical Conductivity of Blood and Serum in Acute *Trypanosoma brucei* Infection.**—*Jl. Comp. Path. & Therap.* 1937. Sept. Vol. 50. Pt. 3. pp. 195–200. With 1 fig. [16 refs.]

This work was undertaken in order to ascertain whether any marked change exists in the electrical conductivity of the serum or blood of nagana rats during the progress of the disease in comparison with normal rats.

It was found that there was a distinct difference in conductivity in the case of normal and nagana defibrinated rat blood, that of the infected blood being definitely higher than that of the normal blood. Normal and nagana rat serum exhibited no difference in conductivity. The conductivity of normal and nagana serum is always higher than that of serum which contains blood cells or *T. brucei*. The lower conductivity of the cells is apparently due to their physico-chemical structure and the relative impermeability of the cell wall to the ions.

W. Y.

SHARROCKS (Horace F.). **The Action of Specific Immune Serum and of Normal Human Serum on Infections of *Trypanosoma hippicum* Darling in the Rat.**—*Univ. California Public. Zoöl.* 1937. Vol. 41. No. 18. pp. 235–248. [17 refs.]

The following summary is given :—

" 1. An improved method of separating trypanosomes from the blood constituents of the host is described. The technic calls for a potent hemolytic serum specific for all the blood cells of the host which is used for agglutination of the mass of the blood cells, followed by hemolysis of the remaining constituents.

" 2. The isolated trypanosomes were used as antigen in the production of two specific antitrypanosome sera. The production of one serum was stimulated by injecting rabbits with living trypanosomes ; the other, with organisms killed by 0·5 per cent. phenol.

" 3. Titres of both trypanolytic sera were virtually identical with regard to the strain used in immunization when tested *in vitro* (agglutination and lysis) and *in vivo* (protection).

" 4. The serum produced against living trypanosomes was of a more polyvalent nature (*i.e.*, it was antagonistic to more strains) than the phenolized antigen serum when tested *in vitro* against several heterologous strains of the same species.

" 5. Protection experiments showed that the survival time of treated protected rats, contrary to the conclusions of Taliaferro and Johnson (1926) and Johnson (1929), was in direct proportion to the amount of protective immune serum administered.

" 6. Experiments showed that with periods of 72 and 144 hours elapsing between two doses of the same pooled sera, a crisis was induced after the second injection of serum. This seems to indicate that the trypanosomes were not completely resistant to the action of this serum even though they had survived former contact with it. This is in contrast to the results of Franke (1905) and many later investigators, who have reported that when trypanosomes once resist the action of a serum, they are resistant for numerous generations to further action of that same serum.

" 7. Pooled normal human serum was titrated under the same condition as the immune sera referred to above, and showed partial destruction of the trypanosomes at a dilution of only 1 : 64. *In vivo*, however, 1·0- and 2·0-cc. doses gave complete protection to rats whose controls died in nine days. Laveran and Mesnil (1912) and other early workers believed the definite *in vivo* action of normal human serum could

not be demonstrated *in vitro*. Yorke, Adams, and Murgatroyd (1929, 1930) state that there is a direct action of the human serum on a suspension of the organisms *in vitro*. Several workers since then have shown that this direct action of the human serum does not protect even man himself from infection by a strain susceptible to the same human serum *in vitro*. The present work, by comparing specific immune sera of high titre with normal human serum of low *in vitro* titre, confirms the recent view that there is a slight *in vitro* action of human serum on the organisms, yet shows this is not responsible for the complete protection afforded rats when normal human serum is administered." *W. Y.*

VAN DEN BRANDEN & POTTIER (R.). Le controle biologique des glyphenarsines (tryparsamide, tryponarsyl, novatoxyl, trypothan). [**The Biological Control of the Glyphenarsines (Tryparsamide, Tryponarsyl, Novatoxyl and Trypothan.**]—*Bull. Soc. Path. Exot.* 1938. Jan. 12. Vol. 31. No. 1. pp. 46–52.

The authors point out that hitherto all tests on the toxicity of the glyphenarsines have been carried out successfully on rabbits. Recently, however, they have substituted the white rat. Their technique is as follows :—

Five white rats, preferably males (if not, non-gravid females), weight 100–150 gm. and free from all visible blemishes, are given 1·5 gm. of the drug per kilo. of body weight. This dose is dissolved in 10 times its weight of distilled sterile water, and the solution is injected into the caudal vein. It is laid down that during the 6 following days not more than 2 rats should succumb, and the remainder should exhibit all the appearances of good health.

Thirty-two comparative tests were made on rabbits and white rats simultaneously, and of these 30 gave concordant results. The authors conclude, therefore, that for glyphenarsine toxicity tests the rabbit can be replaced by the white rat.

In order to render the biological control of the glyphenarsines still more severe, the authors have practised the toxicity tests on rabbits infected with *T. brucei* when the infection has become chronic, thus approaching as closely as possible the conditions met with when man is treated with tryparsamide. The maximum duration of *T. brucei* infection in rabbits is 58 days, and in order to prolong the infection beyond this period small doses of fouadin were given from time to time. By this means 18 rabbits were kept alive during a period of 5 months.

Glyphenarsine toxicity tests on such chronically infected animals revealed no differences from those performed on normal animals. The general conclusions reached were that if the glyphenarsines submitted to these tests produce visual troubles in abnormal numbers, or other ill effects, the cause must be attributed to the state of the patient (intercurrent infections, exhaustion, etc.), or to faults of technique. *W. Y.*

WITTEBOLLE (P.). Sur valeur thérapeutique et prophylactique de Dn 18 (trystibine) dans l'infection du cobaye par une souche arséno-résistante de " Trypanosoma gambiense." [**On the Therapeutic and Prophylactic Value of Dn 18 on an Arsenic-Resistant Strain of *T. gambiense* in the Guineapig.**]—*Rev. Belge Sci. Méd.* 1937. June–July. Vol. 9. No. 6. pp. 389-390.

In this note the author records observations on the toxicity and therapeutic value of a trivalent antimonial preparation prepared by

Meurice under the name "Trystibine." The drug had apparently a rapid effect on the peripheral circulation, parasites disappearing from the blood of guineapigs within about ten minutes after the administration of a dose of 2 cgm. per kilo, but the cure was not permanent as relapses occurred.

The general conclusion is that Trystibine (Dn 18) has no prophylactic or permanent therapeutic value for guineapigs infected with *T. gambiense.* *W. Y.*

Launoy (L.) & Prieur (Marie). Etude de l'action trypanocide comparée sur *Tr. brucei, Tr. congolense, Tr. annamense* normal et *Tr. annamense* chimiorésistant de quelques composés organiques d'antimoine. [**Comparison of the Trypanocidal Activity of Seven Organic Antimonial Compounds on** *T. brucei, T. congolense* **and** *T. annamense* **(Normal and Resistant Strains).**]—*Bull. Soc. Path. Exot.* 1937. Dec. 8. Vol. 30. No. 10. pp. 869–871.

A table is given showing the therapeutic activity of four antimonial compounds on mice infected with *T. brucei* and the normal strain of *T. annamense*, respectively. Of the four compounds amino-phenylstibinate of methylglucamine proved to be the best. This compound acted equally well on both infections, producing cures in one-fifth of the toxic dose.

The second part of the work consisted in comparing the action of aminophenylstibinate of methylglucamine on *T. congolense* and on an arsenic-resistant (and therefore antimony resistant) strain of *T. annamense*. It was found that the naturally resistant *T. congolense* and the artificially resistant *T. annamense* responded about equally.

W. Y.

Lagodsky (H.). Toxicité et activité trypanocide (*Tr. brucei*) du chlorure de rhodium, chez la souris. [**Toxicity and Trypanocidal Activity of Chloride of Rhodium in Mice infected with** *T. brucei*.]—*Bull. Soc. Path. Exot.* 1938. Jan. 12. Vol. 31. No. 1. pp. 44–46.

The conclusion reached from this work is that chloride of rhodium is of no therapeutic value in *T. brucei* infections of mice. *W. Y.*

Perla (David). **The Effect of an Excess of Vitamin C on the Natural Resistance of Mice and Guinea Pigs to Trypanosome Infections.**—*Amer. Jl. Hyg.* 1937. Sept. Vol. 26. No. 2. pp. 374–381. [24 refs.]

After summarizing the work of previous investigators showing that the moderate excess of ascorbic acid may raise the natural resistance of guineapigs to diphtheria toxin, the author describes his own experiments on the effect of excess of Vitamin C on *T. equiperdum* infections in mice and guineapigs.

Mice were given 1 mgm. per day of ascorbic acid for 14 days prior to the injection of trypanosomes and thereafter during the course of the infection. This experiment was repeated three times, and each experiment comprised 20 test mice and the same number of control mice. No modification of the infection was observed in any of the experiments.

In another series of experiments the effect of repeated injections of ascorbic acid on *T. brucei* infection in guineapigs was studied. The ascorbic acid was injected intraperitoneally in a dose of 10 mgm. daily. The injections were given during a period of 42 days prior to the infection and thereafter to the death of the animal.

In the first experiment, 12 guineapigs were treated in this way with ascorbic acid and 12 were used as controls. Of the treated animals only two became infected and died within 25 and 30 days; all the controls succumbed.

In the second experiment, the same daily dose of Vitamin C was given during a period of 77 days prior to injection of *T. brucei*. Of the 7 guineapigs treated with ascorbic acid, all succumbed to infection within 11 to 27 days, whilst of the 7 controls 2 failed to become infected. The author concludes from this that the continued injection of 10 mgm. of Vitamin C over a long period may be deleterious and toxic, and may lower the resistance of the host.

In a third experiment, 10 guineapigs were given the daily dose of 10 mgm. of ascorbic acid for 42 days prior to the injection of trypanosomes. All these animals became infected, the average duration of life being 76·3 days; all of the 10 controls also became infected, the average duration of life being 56·1 days.

The author summarizes his work as follows:—

"An excess of vitamin C administered for a period of 2 weeks prior to infection and throughout its course had no influence on the natural resistance of mice to *Trypanosoma equiperdum* infection.

"A moderate excess of vitamin C administered for a period of 6 weeks prior to infection and throughout its course raised the natural resistance to *Trypanosoma brucei* infection in guineapigs of known stock in which the dietary content of vitamin C had been rigidly controlled. These animals either developed abortive infections or if a fatal one supervened lived considerably longer than control animals. This result, however, was not consistently obtained for when ascorbic acid was administered in the same daily quantities for a longer period of time prior to the injection of the trypanosomes, a favourable effect on the course of the disease was not observed."

W. Y.

Talice (R. V.). Nouveaux foyers de la maladie de Chagas. Premiers cas signalés en Uruguay. [**New Foci of Chagas Disease. The First Cases discovered in Uruguay.**]—*Bull. Soc. Path. Exot.* 1937. Dec. 8. Vol. 30. No. 10. pp. 865–869.

Triatoma have been known to exist in Uruguay since 1933, and it was shown in 1921 by Gaminara that *Triatoma infestans* and *T. rubrovaria* were infected with *Trypanosoma cruzi*.

Talice has found that these two species constituted 99 per cent. of the Triatoma of this region; their habits differ markedly. *T. rubrovaria* is not a domestic insect; it lives on rocky hillocks and feeds on the blood of wild animals, and exceptionally on that of man. *T. infestans* is, however, strictly domestic, it is never found far from human habitations and feeds on man and his domestic animals.

Up to the commencement of this year, an infected vertebrate animal had not been found. Encouraged by the success of the Argentine workers and being convinced that *T. infestans* must play the most important part in the dissemination of the trypanosome, the author commenced a study of this bug, and searched carefully for

cases of human infection in the department of Paysandú, where *T. infestans* is very prevalent. His work was rewarded by the discovery of 4 cases of the disease, *viz.*, a girl aged 8, a man of 20, a girl of 12, and a child of 4. Clinical details of these cases are given. *W. Y.*

TALICE (R. V.), RIAL (Benito), VOLONTERIO (Mario) & OSIMANI (Juan J.). Segundo caso uruguayo de enfermedad de Chagas (forma aguda). [**Another Acute Case of Chagas' Disease in Uruguay.**]—Reprinted from *Archivos Uruguayos de Med., Cirug. y Especialidades.* 1937. Nov. Vol. 11. No. 5. pp. 493–506. With 4 figs. & 1 chart. [11 refs.]

This is the second case of Chagas' disease in an acute form to be recorded in Uruguay. The first was diagnosed in the same town, Paysandú, by Talice, DE MEDINA and Rial in April, 1937.

The patient whose case is described here was a girl of 12 years who lived in Buricayupí and came to the Paysandú hospital for treatment and was admitted. *Triatoma infestans* abounded in the patient's home. The course was typical and the patient left hospital ten weeks later. The dacryo-adenitis was very distinct (see illustration). The blood showed little change in the erythrocyte count, but the leucocytes a month after admission were 4,600 per cmm., with 52·5 per cent. lymphocytes; sixteen days later 10,700 of which 62·1 per cent. were lymphocytes, and a fortnight later (10 days before the patient left hospital), 19,300 with 58 per cent. lymphocytes. Her serum gave a positive W.R. at the first examination [no record is found of later tests], though there were no other indications of syphilis and the mother's blood gave a negative W.R. The authors wonder whether Chagas' disease may cause this reaction.

Left eye of patient with Chagas' Disease, showing dacryo-adenitis. (The patient is looking towards her nose).

[Reproduced from the *Archivos Uruguayos de Medicina, Cirugía y Especialidades.*]

H. H. S.

Mazza (Salvador), Basso (Germinal) & Basso (Redento). Investigaciones sobre la enfermedad de Chagas. I. Primer caso mortal de forma aguda de enfermedad de Chagas comprobado en Mendoza. [**First Fatal Case of Acute Chagas' Disease in Mendoza.**] —*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina Jujuy.* 1937. Publicación No. 33. pp. 1–32. With 30 figs.

The patient was a girl of 12 years, living in Guaymallén, in which district all her life had been spent. The first sign of her illness was on 24th April, 1936, when she had oedema and itching of the lids of the right eye; by the 29th the oedema had occluded the eye and spread to the cheek and temporal region. The skin over it was of a violet-red colour; the submaxillary and cervical glands of the same side were enlarged, but not the pre-auricular, 17 days after the onset. The liver extended from the 5th interspace to two fingers'-breadths below the costal margin, and the spleen three. Five or more trypanosomes could be found in each thick drop of blood. The cardiac area was normal, pulse regular, 99 per minute. There seemed to be slight increase in the size of the thyroid. On 20th May vomiting occurred; two days later the pulse rate was 120, with marked hypotension; red cells 3,980,000, white 6,400, Hb 65 per cent. On the 23rd she was sleepless and restless, with bilious vomiting and epigastric pain; the next day the pain was worse and extended to the precordium; tonic contractions supervened, with cyanosis, loss of consciousness and failing pulse, death occurring 30 days after the initial symptom. Necropsy was carried out within 24 hours and the findings as detailed were typical [see this *Bulletin*, 1937, Vol. 34, p. 280] and are illustrated in a series of good microphotographs. *H. H. S.*

Ciotola (Enrique). La ontogenia del Tripanosoma Cruzi. La enfermedad de Chagas. [**The Ontogeny of** *T. cruzi*. **Chagas' Disease.**]—*Prensa Méd. Argentina.* 1937. May 19. Vol. 24. No. 20. pp. 1025–1038. With 9 figs.

The author states that he has seen a number of cases of Chagas' disease in Peru and has studied the development of the trypanosome in the blood of a patient and in inoculated guineapigs. The multiplicity of forms which he considers the trypanosomes assume can lead only to one conclusion, namely that he has included in the life cycle almost every object other than normal leucocytes or red blood corpuscles which may be found in blood films not too carefully prepared. The author is evidently dealing with a subject with which he is quite unfamiliar. *C. M. Wenyon.*

Kofoid (Charles C.), McNeil (Ethel) & Wood (Fae D.). **Effects of Arsenicals on** *Trypanosoma cruzi* **in Tissue Culture.**—Reprinted from *Jl. Pharm. & Experim. Therap.* 1937. Apr. Vol. 59. No. 4. pp. 424–428.

It has been found that *Trypanosoma cruzi* will undergo cyclical development in tissue cultures of 14 to 16-day embryonic rat heart. Since both the mammalian phase, including blood and tissue forms,

and culture forms typical of the insect phases of *T. cruzi*, are present in the tissue cultures, these preparations offer a useful medium for testing and observing the effects of trypanocidal drugs.

It was found that tissue cultures of embryonic rat heart in rat plasma and rat embryo extract showed blood forms of the trypanosomes about the 5th day after inoculation. Consequently, it was considered best to add the drugs to be studied to the cultures on that day. Of the three arsenicals tested, *viz.*, arsenious tri-thiosalicylic acid, ultra-violet-irradiated tryparsamide, and ultra-violet-irradiated carbarsone, the first proved to be far the most toxic for *T. cruzi*, but previous experiments had proved that this compound is likewise toxic to tissue *in vitro*, and also that it is highly toxic to mammals. Details of the experiments are given. *W. Y.*

Wood (Sherwin F.). **Cytological Variations in the Blood and Blood-forming Organs of White-Footed Mice experimentally infected with** *Trypanosoma cruzi*.—*Univ. California Public. Zool.* 1937. Vol. 41. No. 26. pp. 389–417. With 27 figs. (19 coloured) on 3 plates. [68 refs.]

The author summarizes his observations as follows :—

" 1. The normal blood of the white-footed mouse (*Peromyscus*) includes orthochromatic and polychromatic red corpuscles, neutrophil, eosinophil, and basophil leucocytes, lymphocytes, mononuclears, and platelets.

" 2. An increased number of large lymphocytes in the peripheral blood from fourteen to thirty-six days after inoculation was produced by experimental infection with *Trypanosoma cruzi*, California strain.

" 3. The eosinophil leucocytes were decreased in number from twenty-six to thirty-six days after inoculation.

" 4. The histology of the normal spleen of *Peromyscus* is described.

" 5. Infected mice showed enlargement of the spleen up to twice normal size.

" 6. Enlarged bronchial, lumbar, and inguinal lymph nodes were found in infected animals.

" 7. Hyperplasia of the lymphoblasts and lymphocytes of the follicles in the spleen, resulting in increase in size of the follicles from three to five times normal, was observed in animals killed twenty-one to twenty-seven days after inoculation.

" 8. Myeloid metaplasia was noted in the spleen of some mice, involving increase of erythroblasts and eosinophil myelocytes.

" 9. Megakaryocytes were increased in sections of spleen and sternal marrow of infected animals.

" 10. Hyperplasia of the reticulo-endothelial cells of the spleen was produced in white-footed mice by experimental infection with the California strain of *Trypanosoma cruzi*."

W. Y.

Erratum.

Rhodesia, Southern. **Report on the Southern Rhodesia Trypanosomiasis Committee and Bureau** [Brain (Chas. K.), Vice-Chairman]. —22 mimeographed pp. With 1 folding map. 1937. Jan. 9.

Mr. Rupert W. Jack, Chief Entomologist, Department of Agriculture, Southern Rhodesia, has written calling attention to an error in the summary of the above report which appeared in the

Tropical Diseases Bulletin, 1937, Vol. 34, No. 12, p. 917. In the summary it was stated that " A scheme of tsetse fly research submitted by the Chief Entomologist was considered, but the Committee did not feel justified in giving the scheme its unqualified support." Mr. Jack points out that the Committee in reporting on the scheme of Tsetse Fly Research submitted by him unanimously approved his programme of research and recommended that the work be put in hand as soon as possible. The scheme to which the Committee did not feel justified in giving its unqualified support was one drawn up by Mr. J. FYNN for Tsetse Control by reclamation and development of Africa.

THE TYPHUS GROUP OF FEVERS.

BURNET (Etienne). Les rickettsioses humaines. Rapport présenté au VIIIe Congrès de la Fédération des Sciences Médicales de l'Afrique du Nord (Alger, 22–24 mars 1937). [**Rickettsial Diseases in Man.**]—*Arch. Inst. Pasteur de Tunis.* 1937. June. Vol. 26. No. 2. pp. 391–402.

A report presented to the 8th Congress of the Federation of Scientific Medical Societies in N. Africa held at Algiers in March 1937.

The author defines the human rickettsial diseases as those caused by Rickettsia which are pathogenic for man and animals, and found also in invertebrates such as lice, fleas, ticks and mites; in true typhus man is principally involved, whereas in the other typhus-like diseases man is only occasionally involved. In most of these diseases the parasites can only be directly demonstrated in the rodent host or the insect vector.

The following provisional classification is proposed :—

RICKETTSIAL DISEASES.

Group I. Type—Typhus.

Vector—		
Lice	Subgroup A.	Historic (Epidemic typhus)
Lice & fleas	,, B.	Mexican typhus, Tabardillo, Brill's disease.
Flea	,, C.	Murine typhus Shop typhus, Malaya Ship typhus, Toulon Murine typhus in Greece, Morocco, Tunis, etc. Mouse typhus, Tunis.

Group II. Type—Spotted Fever.

Vector—	
Ticks	Rocky Mountain fever São Paulo fever Fièvre boutonneuse Tick bite fever, S. Africa.

Group III. Type—Japanese River Fever.

Vector—	
Mites	Tsutsugamushi fever Scrub typhus, Malaya.

Group IV. The recurrent Rickettsioses.

Lice	Trench fever Malady of Weigl.

Group V.

Lice	Trachoma.

Each group and the individual diseases included were passed in review. In the discussion it was pointed out that as tabardillo in Mexico was carried from the rat to man by rat fleas this disease should be placed in subgroup C.

A full discussion of the evolution and origin of the Rickettsia followed. The author suggests that the original home of these parasites was possibly in the burrow of a small rodent in Eastern Asia and

transmitted towards the west by human migration, clothes and lice multiplying as the colder climates were reached. From the Old World typhus was carried to the New and with the Malayan migration completed the circuit of the globe. *D. Harvey.*

Bulletin of the Health Organisation. (League of Nations.) 1937. Apr. Vol. 6. No. 2. pp. 205–222.—**The Prophylaxis of Typhus Fever and Vaccination against that Disease : I. Introduction. II. Report on the Consultation of Experts. Annexes.**

The first part of this report consists of a review of the present position of vaccination against typhus, especially with regard to the use of a living vaccine by the methods of Blanc, Laigret and others.

The Spanish Government, in view of the grave risk of the outbreak of typhus among troops and refugees, had asked the League for technical advice regarding measures of protection. A mission was accordingly sent to Spain to investigate the situation; they reported that so far as they could discover typhus had not yet broken out, although conditions favoured an outbreak. A committee of experts was assembled and held several meetings in Geneva during February 1937.

The Committee reported that :—

(*a*) Living virus vaccines conferred an early protection against typhus, whether by premunition only or by premunition followed by immunity.

(*b*) Living virus vaccines, provided they actually induced infection, conferred greater and hence wider protection than did killed vaccines, *i.e.*, mild strains of living virus can protect against infection with virulent strains.

The Committee were also of opinion that in the presence of an epidemic the risks involved in the use of living virus vaccines could be disregarded; on the other hand in a country free from typhus, but where the disease was a menace, killed vaccines were indicated in spite of their increased cost and lesser efficacy as their use did not involve the introduction of a living virus into a country which was at the time free from it.

The experts were agreed that the use of vaccines did not make the standard lousing methods unnecessary, indeed they considered that lousing was of primary importance and should be organized and carried out amongst troops and civilians before typhus had actually broken out; thorough training of lousing staffs being considered essential to its success. Early detection of cases, the isolation of cases and the collection of serum from convalescents were also emphasized.

D. H.

Shortt (H. E.). Les maladies du genre typhus dans l'Inde. [**Typhus Fevers in India.**]—*Bull. Office Internat. d'Hyg. Publique.* 1937. Nov. Vol. 29. No. 11. pp. 2314–2327. [14 refs.]

This report to the International Hygiene Bureau is a review of the papers written by the author and others in the last few years dealing with typhus fevers in India generally and in the Simla Hills in particular. These reports and papers have already been reviewed in this *Bulletin*, 1935, Vol. 32, p. 172; 1936, Vol. 33, pp. 417–20, 909; 1937, Vol. 34, pp. 471–72. *D. H.*

Smith (R. O. A.) & Mehta (D. R.). **Studies on Typhus in the Simla Hills. Part VII. Attempts to isolate a Strain of XK Typhus from Wild Rats.**—*Indian Jl. Med. Res.* 1937. Oct. Vol. 25. No. 2. pp. 345–351. [10 refs.]

As already reported by Covell and Mehta a murine typhus virus has been isolated from wild rats caught in or near Kasauli and a similar virus *OX19* has been isolated from fleas caught on these rats.

Two waves of typhus are met with in the Simla Hills, one occurs in the winter—the sera of these cases agglutinate *Proteus OX19*—the other occurs just after the monsoon in August, September and October—the sera of these cases agglutinate *Proteus OXK*.

The present research was carried out with a view to the isolation of the virus of the *OXK* variety and the carrying out of transmission experiments with ticks and mites. The sera of 1,212 wild rats, captured from May 1935 to February 1936, were tested for agglutinins and the results are given in tubular form. It is of interest to note that there was a marked increase during the months of October, November and December of sera which agglutinated *OXK* in significant dilutions; that is in the period just after the maximum incidence of cases of this type of the disease was recorded.

Two of the rats showing agglutinins in high dilution for *OXK* were selected and mites *L. bacoti* were collected from them and emulsified and injected into guineapigs but without result.

Fleas of the genus Nosopsyllus (Ceratophyllus) were fed on these rats and later emulsified and injected into a normal guineapig but without result. A nymph of the tick *Rhipicephalus sanguineus* was found on one of the rats. It was allowed to engorge and later removed. The adult tick was emulsified and injected but without result. The rats were then killed and the brains and spleens removed and injected into guineapigs but also without result.

With a view to seeing if any change resulted in the nature of the virus (*OX19*) when transmitted by ticks or mites numerous ticks and larval mites were fed on guineapigs and rats infected with the local *X19* virus; they were then emulsified and injected into other animals but without producing any infection. It is interesting to note that when fleas *N. simla* were fed on the same infected animals and later injected into guineapigs they produced the typical infection of a murine virus fever and orchitis with production of agglutinins in rabbits for *OX19*.

In August and September when cases of the *OXK* type of fever were occurring and fleas were very numerous on the rats collected, fleas were taken from these rats, emulsified in batches and injected into guineapigs. A murine virus *X19* was isolated on 3 occasions but no virus of the *OXK* type. *D. H.*

Mehta (D. R.). **Studies on Typhus in the Simla Hills. Part VIII. Ectoparasites of Rats and Shrews with Special Reference to their Possible Rôle in the Transmission of Typhus.**—*Indian Jl. Med. Res.* 1937. Oct. Vol. 25. No. 2. pp. 353–365. With 2 charts. [16 refs.]

Two thousand four hundred and fifty-one rodents, rats, mice and shrews, were trapped in and around Kasauli in the Simla Hills in the year 1935–6. These were investigated as regards the ectoparasites

and these were identified and careful records made in relation to the seasonal numbers. The results are fully set out in tables and charts. An interesting point is that at the time (cold weather) when the maximum of the murine typhus cases (*X19*) occurs the flea population is at its minimum on the rats ; and when the *OXK* cases occur in the months just at the end and after the monsoon August, September and October, fleas, lice and ticks on rats and other rodents are at a maximum.

Amongst the arthropods occurring as external parasites and identified by the author were included the fleas *X. cheopis*, *Nosopsyllus simla*, *C. canis* and *C. felis*. The principal mites studied were *L. bacoti* and larval forms of *Trombicula deliensis*. Ticks were represented by the larvae and nymphs of *Hyalomma aegyptium*, *Rhipicephalus sanguineus* ; lice *Polyplax spinulosa*.

The possible rôle of fleas, mites, ticks and lice in the transmission of typhus in the Simla hills is discussed and it is emphasized that the larval mites and the Hyalomma tick may possibly be concerned in the transmission of the rural type (*OXK*) of typhus. Experiments are now in progress with a view to the isolation of the *OXK* virus (see previous paper) and its transmission by ticks and mites. *D. H.*

Yacob (M.). **A Note on a Circumscribed Outbreak of a Typhus-like Fever in Muzaffargarh District, South-Western Punjab.**—*Indian Med. Gaz.* 1937. Oct. Vol. 72. No. 10. pp. 585–586.

An outbreak of fever was reported in two small jungle villages of about 50 inhabitants. Eleven cases of the fever were seen and investigated.

A history of a primary necrotic sore with enlarged glands was reported in all the cases with a very definite rash. In one instance the friend of one of the patients cut his finger and applied the bleeding point to the primary sore on the hand of the patient, a few days later he developed a typical sore on the finger with lymphangitis and lymphadenitis ; he had high fever which lasted 14 days with a well marked rash. The Weil-Felix reaction for *Proteus OX19* was positive in 6 out of 7 cases tested but only in low dilutions, *Proteus OXK* was not agglutinated. *D. H.*

Kapila (C. C.) & Maitra (G. C.). **A Severe Case of Scrub Typhus.**—*Indian Med. Gaz.* 1937. July. Vol. 72. No. 7. pp. 417–418. With 1 chart.

The fever in this case lasted for 3 weeks and the temperature chart resembled that of a typhoid case. No primary ulcer was detected but swollen and tender glands were noted in the axilla, in the neck and in the inguinal region. On the 6th day an erythematous rash developed and faded in a week leaving a dusky mottling. A positive Weil-Felix reaction with *OXK* was obtained on the 15th day of the fever.

D. H.

Hassett (C. J.). **A Case of Indian Typhus.**—*Indian Med. Gaz.* 1937. Nov. Vol. 72. No. 11. pp. 679–680.

A very severe case of fever with delirium and unconsciousness for 5 days with symptoms of meningitis ; retraction of the head, rigidity

of the neck muscles and Kernig's sign positive. A profuse macular rash developed on the body and spread to the face and palms of hands and soles of the feet. The Weil-Felix reaction was positive in a dilution of 1/1000 for *Proteus OX19* and *OX2*. The patient later developed a flaccid paralysis of the left arm but this passed off in a few days and he made a good recovery. *D. H.*

Modinos (P.). Les fièvres typho-exanthématiques en Egypte. [**Typhus Fevers in Egypt.**]—75 pp. [110 refs.] 1937. Alexandrie: Imprimerie A. Procaccia.

The first part of this paper consists of a general review of typhus fevers and allied diseases, specially dealing with historic typhus, murine typhus and boutonneuse fever, the 3 members of the group which are met with in Egypt.

Three cases are described in detail: (1) a case of true typhus, (2) a case of murine typhus, (3) a case of boutonneuse fever. These 3 cases came under the personal care of the writer. The sera of cases 1 and 2 agglutinated *Proteus X19* but case 3 gave a negative reaction. Blood taken from Case 2 and inoculated into a guineapig produced fever and orchitis in the animal. A guineapig which had been inoculated with a known typhus virus and had reacted was inoculated later with the virus from Case 2 and was proved to be immune. Controls inoculated at the same time reacted with fever and orchitis. Case 3 was diagnosed as boutonneuse fever for the following reasons: the rash was much more profuse than in Cases 1 and 2 and was definitely papular and the elements could be felt under the skin, at the same time the author considers that "buttons" is not a good description, they are prominent papules; there was a typical primary ulcer on the arm; the Weil-Felix reaction was negative although tested at the same period in the fever as in the other 2 cases which were then positive.

D. H.

Riding (D.). **Murine Typhus in Egypt.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1937. July 31. Vol. 31. No. 2. pp. 255–258. With 1 fig. & 1 plate.

Forty-four wild rats, captured in a village near Cairo where typhus cases had recently occurred, were examined. None of the sera gave a positive Weil-Felix reaction but 3 guineapigs each inoculated from the emulsion of brain of 4 of the rats developed fever with definite orchitis. It has been possible to passage this virus for 12 generations and successful tissue cultures were also obtained. Rabbits inoculated from the infected guineapigs developed a positive Weil-Felix reaction.

D. H.

Riding (D.). Sur le typhus murin en Egypte.—*Bull. Office Internat. d'Hyg. Publique.* 1937. Nov. Vol. 29. No. 11. pp. 2309-2313. With 8 charts.

Durand (Paul). Un cas de typhus murin chez l'homme dans le bled tunisien. [**Murine Typhus affecting Man in Tunisia.**]—*Arch. Inst. Pasteur de Tunis.* 1937. June. Vol. 26. No. 2. pp. 386–390. With 1 fig.

Sparrow and others have shown that many of the rats in the port of Tunis are infected with the virus of typhus, but only one or two cases

of the disease in man have so far been recorded. On the other hand in the country districts around Tunis although over 500 rats were examined none was found to be infected, yet cases of true or historic typhus in man are common ; so far no cases of murine endemic typhus have been recorded in these districts.

In the paper under review Durand describes a case of murine typhus which he has recently discovered. This man was a road surveyor and camped on the roads ; rats were numerous around and in his tent. The fever which lasted 14 days was mild ; there was a profuse rash. The virus was isolated from the patient's blood ; of 16 male guineapigs inoculated all developed fever and 13 also showed orchitis. There was cross immunity in guineapigs with this virus and a historic virus and a murine typhus virus isolated from rats in Tunis, but guineapigs recovered from infection with the virus were not immune to the virus of boutonneuse fever.

The patient's serum gave a positive Weil-Felix reaction in 1/16000 for *Proteus OX19*. *D. H.*

Durieux (C.) & Arquié (E.). Un cas mortel de typhus murin contracté à Dakar. [**A Fatal Case of Murine Typhus in Dakar.**]—*Bull. Soc. Path. Exot.* 1937. July 7. Vol. 30. No. 7. pp. 539–542. With 1 chart

Cases of typhus due to the murine or endemic virus have already been described by the authors as occurring in Dakar ; 4 new cases have since been met with and one of these which proved fatal is detailed in this paper. The patient had high fever with delirium and stupor ; on the 7th day a maculo-papular rash developed and spread over the body, the face and the hands. The Weil-Felix reaction at this stage was positive in a dilution of 1/500 for *Proteus OX19*. The delirium continued and stiffness of the neck, dilatation of the pupil and clonic movements of the limbs developed ; the patient died on the 16th day of the fever. The virus was isolated from the blood of the patient and produced fever and orchitis in guineapigs. The authors conclude that it is not correct to describe endemic typhus as invariably a mild disease ; it may be severe and even fatal as in this case.

D. H.

Gosden (Minnie). **A Suspected Case of Non-Epidemic Typhus in a Child in Trinidad.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1937. Nov. 30. Vol. 31. No. 3. pp. 359–362. With 1 chart.

A case of fatal illness in an African child aged 4 months with a haemorrhagic typhus-like rash and gangrene of the hands. The serum taken post-mortem agglutinated *Proteus OX19* and *OX2* in a dilution of 1/80 ; *Proteus OXK* negative ; all controls with the same cultures were negative. No cases of typhus have been reported in Trinidad for many years and so far no other cases have been seen. *D. H.*

Patino (L.), Afanador (A.) & Paul (J. H.). **A Spotted Fever in Tobia, Colombia. Preliminary Report.**—*Amer. Jl. Trop. Med.* 1937. Sept. Vol. 17. No. 5. pp. 639–653. [10 refs.]

A Yellow Fever Commission was at work in Bogotá, the capital of Colombia, and cases of suspected yellow fever were reported from Tobia, a rural district about 100 kilometres distant. The disease was confined

to the small area of Tobia, one narrow valley 4 kilometres long by 2½ wide ; of the 270 inhabitants of this valley, 63 developed the fever and 60 of these died. Several cases in the acute stage were seen and investigated by members of the Commission. High fever and delirium with marked central nervous manifestations were noted ; the most characteristic symptom was the rash which appeared on the 3rd day and spread over the whole body of the patient ; at first the rash was maculo-papular, later haemorrhagic areas appeared. Albumen was present in the urine.

Laboratory investigations.—Two guineapigs were inoculated with the blood from a case of the disease, both developed fever and both died. Rickettsia were demonstrated in the cells in the peritoneal fluid. This strain of virus was passaged 17 times ; congestion of the testicles was marked and all the experimental animals died. Blood from 6 further cases was injected into guineapigs ; all reacted and all died. Head lice were collected from one patient and emulsified and injected into guineapigs ; these also reacted with fever and died. Rickettsia were demonstrated in the cells in the peritoneal fluid. Lice collected from healthy people gave no reaction when injected, nor did bed-bugs, ticks or mites. Blood cultures from patients were all negative, so also were the Widal and Weil-Felix reactions which were tested at all stages of the fever and in convalescence. All tests for yellow fever were negative. The commission decided that the disease is not yellow fever but resembles São Paulo typhus in some but not all respects, Weil-Felix reaction with *OX19*, *OX2* and *OXK* negative.

A post-mortem examination was carried out in one case, the most marked feature was intense congestion of the meninges.

Rhipicephalus sanguineus, *Amblyomma cajennense* and mites were all found in the valley but in view of the house infection character of the disease (several households were completely wiped out) the authors suggest that an Ornithodorous tick may be the vector. This tick was found in large numbers in the dust in the houses. *D. H.*

Montestruc (E.), Germain (A.) & Clitandre (S.). Premiers cas de typhus endémique bénin diagnostiqués à la Martinique. [**First Cases of Benign Endemic Typhus discovered in Martinique.**]—*Bull. Soc. Path. Exot.* 1937. Nov. 10. Vol. 30. No. 9. pp. 746–749.

Cases of continued fever had been noted in which blood cultures proved sterile and the Widal reaction was also negative. Accordingly the sera of such cases were tested for the Weil-Felix reaction and several positive results were obtained. Two cases are described ; in both instances rats were numerous in the houses.

In one case the fever lasted 12 days and the Weil-Felix reaction was positive in a dilution of 1/1000 for *Proteus X19*. In the other case the fever lasted 14 days and a profuse rash was noted which spread to hands and feet, the Weil-Felix reaction was positive 1/400 with *Proteus X19*, negative with *Proteus OXK*. *D. H.*

Hsieh (T. Y.), Chang (Shih-Lu) & Yang (Chi-Shih). **Typhus Fever in Changsha.**—*Chinese Med. Jl.* 1937. Sept. Vol. 52. No. 3. pp. 383–388.

The earliest report of typhus in China is an epidemic in Shanghai in 1850. Since then periodic epidemics have been reported in the great cities in times of famine and usually accompanied by relapsing fever.

In the present paper 14 cases of typhus are described. These occurred in 1934/6; the cases were moderately severe with high fever but little delirium, and a rash was present in all but one. All cases recovered and convalescence was rapid.

The authors consider that these cases differ from cases of typhus as reported in N. China and may be of the endemic or murine type.

D. H.

Public Health Notes. Adelaide. 1937. July. No. 23. pp. 43–44.—**South Australian Typhus Fever.**

The author states that there is ample evidence that endemic typhus in South Australia is the same as that in other parts of the world. The clinical nature of the illness and the agglutination reactions are the same. Yet although many rats and rat fleas, captured in districts of South Australia where cases of the disease were occurring, have been examined in the laboratory it has not been possible to isolate a typhus virus from any of these. It is suggested that cases of the disease in the early stages should be made available for examination, and indication for the diagnosis of such cases, prior to the appearance of the Weil-Felix reaction, are given. *D. H.*

Bengtson (Ida A.). **Cultivation of the Rickettsiae of Endemic (Murine) and Epidemic (European) Typhus Fever in Vitro.**—*Public Health Rep.* 1937. Sept. 24. Vol. 52. No. 39. pp. 1336–1340. With 1 fig. & 4 plates.

The same methods of culture as were used for the Rickettsia of Rocky Mountain fever were also used to cultivate the virus of endemic and epidemic typhus; Maitland's medium, using Baker's instead of Tyrode's solution. For subculture small portions of the tissue were removed and added to the fresh cultures with fresh minced tissue. Successful subcultures were also made from the fluid without any actual tissue. Seventeen successful subcultures were made. Rickettsia were very numerous in the stained films. Similar results were obtained with the virus of epidemic typhus but the Rickettsia were not so numerous. *D. H.*

Zinsser (Hans), Wei (H.) & Fitzpatrick (Florence). Nouvelles méthodes de culture de *Rickettsiae* du typhus à propos de la production de vaccins. [**Agar Slant Tissue Cultures of Typhus Rickettsia.**]—*C. R. Soc. Biol.* 1938. Vol. 127. No. 3. pp. 229–232. With 1 fig.

Four per cent. agar solution in water is mixed with an equal volume of double strength Tyrode's solution to which 50 per cent. horse serum has been added. The reaction must be *p*H 7·4 to 7·6 and should be maintained at this figure.

Guineapig tunica tissue is finely minced and is infected by immersion in old cultures of typhus Rickettsia. This is then "buttered" on the surface of the agar tubes; in 6 days growth appears. It is proposed to use this method of agar culture in the preparation of vaccines.

D. H.

Noury (M.). Etude et conservation d'une souche de fièvre boutonneuse. [**Preservation of Boutonneuse Fever Virus.**]—*C. R. Soc. Biol.* 1937. Vol. 125. No. 22. pp. 839–841.

A strain of the virus of boutonneuse fever was isolated from a patient by inoculation of blood into guineapigs. One of these guineapigs was killed and an emulsion of the swollen tunica, the suprarenal glands and the spleen was made in 20 cc. of saline solution ; 3·5 cc. of this was inoculated intraperitoneally into another guineapig and this produced fever and marked orchitis. Using this technique the virus has been maintained for more than a year, subinoculations being performed every 5 days. The virus can also be preserved for some months by placing the infected carcase of a guineapig in the ice chest. The reactions in the guineapigs remained uniform throughout ; the incubation period was 2 to 3 days, the orchitis appeared on the 3rd or 4th day and followed immediately after the rise of temperature. This orchitis is more intense and lasts longer than the orchitis due to typhus virus. Guineapigs recovered from the boutonneuse fever were found to be immune to inoculations of the virus of Rocky Mountain Fever. *D. H.*

Blanc (Georges) & Baltazard (M.). Longues conservation à sec du virus de typhus murin dans les déjections de puces infectées. Utilisation de ce virus desséché pour la préparation d'un vaccin contre le typhus exanthématique. [**Long Infectivity of Murine Typhus Virus in Dried Faeces of Infected Fleas.**]—*Bull. Acad. Méd.* 1937. July 27. 101st Year. 3rd Ser. Vol. 118. No. 28. pp. 166–174. With 9 charts. [11 refs.]

It has already been shown that the virus of typhus remains infective for long periods in the dried excreta of lice. The authors repeated these experiments with the excreta of infected fleas and found that if the excreta are carefully dried in vacuo the excreta may be infective for as long as 100 days. They suggest that advantage of this might be taken in the preparation of vaccines as the dried faeces (living virus) could be sent for long distances and could then be treated with bile.

Four volunteers were inoculated with a vaccine prepared in this way and all four were proved to be immunized. Control guineapigs became infected. *D. H.*

Delbove (P.) & Nguyen-Van-Huong. Contribution à l'étude du typhus murin en Cochinchine. Etudes des virus isolés et des immunités qu'ils provoquent. [**Murine Typhus in Cochin-China. Studies on the Virus.**]—*Arch. Insts. Pasteur d'Indochine.* 1937. Apr. Vol. 7. No. 25. pp. 3–26. With 7 charts. [22 refs.]

Two lines of research were followed in this investigation.

1. The characters of the typhus virus isolated from rats in Saigon were studied, and a comparison of the local rat virus with an epidemic typhus virus isolated from a case of typhus in Peking was made.

2. A study of the intensity of the infection in rats and its seasonal variation.

During the years 1933/4 five strains of typhus virus were isolated from rats. Emulsion of the brains of several rats was inoculated into each guineapig. It was only possible to study two of these viruses in detail.

Both were passaged in guineapigs, the one N 15 for 130 passages and the other D 5 for 90 passages. Both produced fever in guineapigs and in 50 per cent. also a scrotal reaction ; cells crowded with Rickettsia were demonstrated in smears made from the inflamed tunica. A rash on the scrotum of the guineapig was also noted in many of these cases.

Cross immunity experiments were carried out with 3 strains of virus N 15 and D 5, the local rat virus strains and the Peking strain of human typhus virus (historic or epidemic). These strains protected guineapigs against the homologous strains, D 5 against D 5 in 80 per cent. of cases, N 15 against N 15 in 86 per cent., and Peking against Peking in 85 per cent. Animals inoculated with N 15 strains were protected against D 5 in 88 per cent. of tests and against Peking in 95 per cent. D 5 was also shown to protect against N 15 and Peking virus and Peking virus protected animals against both the local murine viruses. Thus the 3 strains of virus were shown to be immunologically identical. The sera of 1,015 rats were tested for the Weil-Felix reaction against *Proteus OX19* and *OXK*, between 8 and 9 per cent. of the sera gave a positive reaction mostly with *OX19* but some with *OXK*. It is of interest to note that in November–December the percentage of positive sera rose to 18 per cent. ; in April and May it was 6 per cent. and in June 20 per cent. The average over the year as already noted was 8 to 9 per cent. *D. H.*

Delbove (P.). Le typhus murin à Saigon. Immunité croisée avec le typhus épidémique de Chine. [**Murine Typhus in Saigon. Cross-Immunity with the Epidemic Typhus of China.**]—*Bull Soc. Path. Exot.* 1937. Oct. 13. Vol. 30. No. 8. pp. 619–621.

Both urban typhus and scrub typhus (Japanese River fever) occur in Saigon. One thousand three hundred rats were captured in the city and examined ; 8–9 per cent. gave a positive Weil-Felix reaction for *Proteus OX19* and a few agglutinated *OXK*. Strains of virus were isolated from some of these rats and were passaged. Crossed immunity experiments were carried out and it was shown that this murine strain of Saigon protected guineapigs against infection with a strain of virus from Peking (epidemic typhus) and also against the homologous virus. *D. H.*

i. Travassos (J.). Sensibilité de la sarigue marsupiale (*Didelphis aurita*) aux inoculations expérimentales du "typhus exanthématique de Sao Paulo." [**Susceptibility of the Opossum to São Paulo Typhus Virus.**]—*C. R. Soc. Biol.* 1937. Vol. 126. No. 33. pp. 1047–1049.

ii. ——. Résultats des inoculations expérimentales sériées du virus du "typhus exanthématique de Sao Paulo" à la sarigue marsupiale (*Didelphis aurita*). [**Inoculation of the Opossum with São Paulo Typhus Virus.**]—*Ibid.* pp. 1049–1053.

iii. ——. Identification d'un virus semblable à celui du "typhus exanthématique de Sao Paulo," isolé de la sarigue marsupiale (*Didelphis paraguayensis*). [**Virus Identical with that of São Paulo Typhus isolated from the Opossum.**]—*Ibid.* pp. 1054–1056.

i. The author succeeded in infecting opossums with the virus of São Paulo typhus recently isolated from a case of the disease.

The animals did not react in any way. There was no fever and no symptoms of illness but when blood was taken from the heart 10 to 18 days after inoculation and injected into guineapigs these animals became infected and gave the typical reactions of São Paulo typhus virus. The infected opossums were killed and examined and "typhus nodules" were demonstrated in or near blood vessels in the liver, lungs and kidneys.

Opossums were also infected with a São Paulo virus which had been passaged for a long time in guineapigs but this virus gave only modified reactions when inoculated into guineapigs from the opossum.

ii. It was also shown that it is possible to passage the São Paulo typhus virus through a series of opossums; 6 passages were obtained. Some modification of the virulence of the virus was also noted here. This may be partly explained by the possibility that some of these opossums had been infected in nature (see below).

iii. Several opossums were captured near São Paulo and examined and from 5 of these a virus was isolated which gave the typical reaction of São Paulo typhus virus in guineapigs. After passage in guineapigs this virus killed about 95 per cent. of the animals inoculated.

Guineapigs which had recovered from the effects of the human virus of São Paulo typhus were immune to the virus isolated from the opossums. Ticks (*Amblyomma cajennense*) were fed on guineapigs infected with the virus derived from the opossum and when fed later on normal guineapigs infected these. Rabbits infected with the virus obtained from opossums developed fever and the sera gave a positive reaction for *OX19*.

It is proposed to carry out further experiments using opossums bred in the laboratory so as to eliminate errors due to natural infection. The writer claims that the opossum is the reservoir or one of the reservoirs of the virus of São Paulo typhus in nature. *D. H.*

Irish Journal of Medical Science. 1938. Jan. pp. 11–19.
—**A Case of Sporadic Typhus, with Some Notes on the Disease.**

A sporadic case of typhus occurring in Cork city where no cases of typhus had been recorded for 8 years. The patient was an architect and in the course of his employment he had to visit slum property in a house in a most insanitary state and in an area which in the old days was known as a typhus district. Ten days later he developed fever and on the 4th day a macular rash appeared on the body and spread to the hands and limbs but not the face. On the 6th day "his appearance was notably dusky. His eyes were suffused and bloodshot and he had a wild distraught appearance. His tongue was dry and covered with a thick brown fur."

The Weil-Felix reaction tested on the 6th, 10th and 20th day of illness was negative. In spite of this and the fact that the temperature fell to normal on the 7th day the case on clinical grounds was diagnosed as typhus. No other cases have been reported in the neighbourhood.

A full discussion of the subject follows and it is emphasized that these sporadic cases probably infected with the rat typhus virus may not give a positive Weil-Felix reaction and must be diagnosed on clinical grounds alone. Practitioners should be on the outlook for such cases. It is also suggested that investigation of the local rat population might reveal the existence of a focus of typhus infection.

Some very interesting historical records of famine and jail fever are included. *D. H.*

Aubaret. Fièvre exanthématique à inoculation palpebrale. [**Typhus Infection viâ the Eyelid.**]—*Bull. Soc. Path. Exot.* 1937. Dec. 8. Vol. 30. No. 10. pp. 832–834.

A patient who was seen on 20th August, 1936, had a small ulcer on the margin of the lower eyelid of the left eye ; there was no conjunctivitis but swollen and painful glands were noted in front of the ear and at the angle of the jaw. Temperature was normal but the patient complained of feeling weak and tired. She stated that on the 12th August she had crushed a tick removed from a cat and that some of the content of the tick had splashed into her eye. Two days later she noticed a small pimple on the eyelid. The patient was admitted to hospital and although the temperature remained at or about normal a typical boutonneuse fever rash developed a few days later. The ulcer healed rapidly and disappeared two days after the appearance of the rash which persisted for some weeks. The interesting point in this case was that the primary sore, a minute ulcer, occurred on the eyelid and was accompanied by involvement of the neighbouring lymph glands yet there was no inflammation of the eye. *D. H.*

Raybaud (A.). Tache noire et fièvre boutonneuse. [*Tache noire* **and Boutonneuse Fever.**]—*Bull. Soc. Path. Exot.* 1937. Oct. 13. Vol. 30. No. 8. pp. 624–627.

The author considers that the tache noire is diagnostic in boutonneuse fever but asks can one diagnose a case of fever in which the primary sore is present but in which there is no rash, *i.e.*, " boutonneuse fever sine bouton" ?

Three typical cases are reported with rash and primary sore ; the wife of one of these patients developed fever with a typical primary sore but no rash and still another case is reported of the same type. That is, 5 cases of boutonneuse fever were observed at the same time and in the same families, 3 of them had fever, rash and primary sore, 2 had fever and primary sore but no rash. *D. H.*

Sparrow (Hélène) & Roussel (Henri). Recherche du *Proteus X19* dans le sang de sujets typhiques et non typhiques. [*Proteus X19* **in the Blood of Typhus Patients.**]—*Arch. Inst. Pasteur de Tunis.* 1937. June. Vol. 26. No. 2. pp. 257–265.

In 1935 in a small outbreak of typhus, the authors carried out blood cultures in all the cases and in 50 per cent. of the cases *Proteus X19* was isolated [see this *Bulletin*, 1936, Vol. 33, p. 434]. This result was so unusual that the writers repeated the work in 1936. 565 blood cultures were made, these were from samples of blood sent to the laboratory for the Weil-Felix reaction. The serum was used for this and the clot placed in the culture medium. 348 of these samples of blood were from typhus cases, 309 gave a positive Weil-Felix reaction and *Proteus X19* was isolated 10 times or in 2·8 per cent. of the cases.

One hundred cultures were made from cases of fever other than typhus and in 6 instances *Proteus X19* was isolated, 6 per cent. All the strains isolated gave the true reaction of *X19* and the cultures were agglutinated in high titre by specific serum from cases of typhus and from laboratory animals. In view of the high percentage of positive results in the first outbreak the authors carefully considered the possibility of accidental contamination but definitely exclude this. *D. H.*

Vaucel (M.) & Bruneau (M.). Isolement, des rats de Hanoi, d'une souche de *Proteus OXK*. [**Isolation of *Proteus OXK* from Rats in Hanoi.**]—*Bull. Soc. Path. Exot.* 1937. June 9. Vol. 30. No. 6. pp. 448–450.

Four per cent. of rats captured in Hanoi gave a positive Weil-Felix reaction for *Proteus OXK*.

During the year 1936, 288 blood cultures were made from rats captured in the town; from these cultures 22 strains of *Proteus* were obtained; only one of these, however, was fully identified as identical in cultural and serological tests with *Proteus OXK*. *D. H.*

Giroud (Paul) & Tannenbaum (Simon). Faits concernant la réaction de Weil et Félix. [**On the Weil-Felix Reaction.**]—*C. R. Soc. Biol.* 1937. Vol. 125. No. 21. pp. 698–700.

The authors consider that the production of agglutinins for *Proteus* during typhus infection in man and in some experimental animals is due to the invasion of the blood stream by that bacillus. *Proteus* is a common inhabitant of the intestine of man and of rabbits but is not found in the intestine of guineapigs, the serum of these last does not show a positive Weil-Felix reaction.

The authors fed guineapigs on milk infected with *Proteus*; the blood when tested did not show any agglutinins, but when the same animals were infected with typhus virus the serum gave a positive Weil-Felix reaction with *Proteus OX19* and *OX2* but not with *Proteus OXK*.

The authors suggest that the Weil-Felix reaction is due to the passage of *Proteus* from the intestine into the blood during an attack of fever, and that guineapigs do not give a positive Weil-Felix reaction because *Proteus* is not present in their intestine. *D. H.*

Bonjean (M.) & Nain (M.). La réaction de Weil Felix chez les sujets vaccinés contre le typhus par le vaccin bilié de Georges Blanc. [**The Weil-Felix Reaction in People vaccinated against Typhus with Bile-treated Vaccine.**]—*C. R. Soc. Biol.* 1937. Vol. 125. No. 23. pp. 998–1000.

The blood of 111 persons who had been recently vaccinated against typhus was tested for the Weil-Felix reaction. Fifteen cases were negative, the remaining 96 cases showed a positive reaction varying from 1/25 to 1/500. *D. H.*

Parrot (G.). Les rickettsioses confèrent-elles l'immunité vraie ou la prémunition? [**Does True Immunity or Premunition result from Rickettsia Infection?**]—*Arch. Inst. Pasteur d'Algérie.* 1937. June. Vol. 15. No. 2. pp. 188–213. [89 refs.]

The author distinguishes between premunition and true immunity as follows. In certain diseases such as scarlet fever, typhoid, etc., when the patient recovers from the disease the germ disappears entirely from the system, and the patient is resistant to further infection with the same parasite, this is true immunity. On the other hand in certain diseases such as malaria, syphilis, trypanosomiasis, piroplasmosis, etc., the clinical symptoms of the disease may disappear and the patient be apparently in good health yet the germ is still in the system and as long as the germ remains in the system the individual is resistant to fresh infection. This is premunition. However, if a complete cure

follows and the parasite disappears entirely from the system a true immunity may follow, or on the other hand reinfection may take place.

Maladies of premunition differ from immune maladies in that in the first case the virus remains in the body for a long time after the disappearance of clinical symptoms. In premunition diseases the reticulo-endothelial system is involved as is evidenced by the proliferation of these cells and the fact that splenectomy is often followed by relapse in such diseases as malaria, piroplasmosis and Bartonelloses. Also relapses of malaria may occur in a patient after a cold bath or when other diseases interfere with the reticulo-endothelial system.

In premunition diseases also if reinoculation occurs there may be (*a*) no result, (*b*) relapse with fever and reappearance of parasites in blood, (*c*) no fever but relapse of parasites. Also in premunition there may be no initial attack of fever, the parasites gaining admission to the blood and lodging in the spleen, later on when resistance is lowered an attack of fever may result ; thus people may spend some years in Africa and never have had an attack of malaria, but on arriving home in England in winter they may develop a severe attack of fever ; these people have been living in Africa in a state of premunition.

The persistence of living organisms in the body is necessary for resistance to infection with premunition diseases, therefore vaccines for typhus must be prepared with the living virus.

The proof of the state of premunition is isolation of the parasite or detection of the parasite in the body of a person who has had the disease and is resistant to it. In malaria this detection is easy but in typhus direct detection of the Rickettsia in the blood is exceedingly difficult.

Discovery of the virus is by indirect methods : (1) by inoculation of blood or tissues into susceptible animals ; (2) by feeding lice, fleas or ticks on animals ; (3) by splenectomy or blocking of the reticulo-endothelial system followed by relapses.

By employing these methods certain rickettsial diseases have been shown to be followed by a condition of premunition, that is the parasite can be recovered from the animal long after the disease has disappeared and the animals are resistant to further infection.

Such diseases are the rickettsial diseases of dogs, sheep and cattle including heart water, also trench fever in man. By analogy it is suggested that in other rickettsial diseases of man, such as Japanese River fever, Rocky Mountain fever, murine typhus, the same applies and these diseases also fall into the category of premunition diseases. It is also suggested that in non-epidemic periods when no cases of clinical typhus are occurring, if the virus is latent in the bodies of certain people, some interference with the functions of the reticulo-endothelial system may result in a parasitic relapse and infection of lice, thus forming a starting point for an epidemic outbreak in the next season. *D. H.*

Castaneda (M. Ruiz). **The Rôle of the Body Temperature in Experimental Typhus Infection. Generalized Rickettsial Infection of the Peritoneum in Guinea Pigs, Rabbits and Sheep.**—*Jl. Immunology.* 1937. Aug. Vol. 33. No. 2. pp. 101–110. With 1 chart.

Zinsser and Castaneda working in the Harvard laboratories found that by irradiation of infected rats they were able to obtain large

numbers of rickettsial bodies in the peritoneal fluid and were thus able to prepare vaccines from this fluid. This work was repeated on the same lines in Mexico City but without success. Castaneda in the present paper shows that the reason for the failure was that in infected rats in Mexico City the temperature was over 39°C. He finds that if rats and rabbits or guineapigs are infected with typhus virus and the temperature is kept under 38°C. large numbers of Rickettsiae appear in the peritoneal fluid, whereas if the temperature rises above that figure very few Rickettsiae can be seen.

The practical application of these studies to the preparation of typhus vaccine is being considered. *D. H.*

Noury (M.). Essais d'immunisation contre le typhus exanthématique par des doses répétées de vaccin tué. [**Immunization against Typhus by Killed Vaccine.**]—*C. R. Soc. Biol.* 1937. Vol. 125. No. 22. pp. 849–850.

An emulsion of the brain of a guineapig infected with murine typhus was prepared of a strength of 5 per cent. in 1 per cent. carbolic; this was stored in the ice chest. Daily injections of 1 cc. of this emulsion were given to 12 guineapigs over a period of 1 month; when tested none showed any evidence of protection. Another batch of 7 guineapigs were given a similar course of injections. These were tested 30 days after the last dose of vaccine; none was protected.

The author's conclusions are that killed vaccines do not protect; living vaccines are necessary for immunization. *D. H.*

Schäfer (Walther). Zur Frage der Schutzimpfung gegen Fleckfieber. (Immunisierungsversuche an weissen Mäusen mit Impfstoffen nach dem Verfahren von Laigret und Durand.) [**Concerning Vaccination against Typhus. Immunization of White Mice by the Method of Laigret and Durand.**]—*Arb. a. d. Staatsinst. f. Exp. Ther. u. d. Georg Speyer-Hause zu Frankfurt a.M.* 1937. No. 34. pp. 39–50.

An extensive research which is fully recorded by means of protocols of experiments.

The main conclusion is that the best results were obtained when the virus was emulsified in yolk of egg and also in oil, and was given in 2 doses; the test doses were then given 24 days later; by this method the mortality in mice was reduced from 66 per cent. to 6 per cent.

When dried vaccine (brain of infected guineapigs) was emulsified in yolk of egg only, the protection afforded was not nearly as good; it is suggested that this may be due to destruction of the virus by the drying process, it is only when living vaccine is injected that protection results. *D. H.*

i. Okamoto (Yutaka). **Experimental Studies on Mice concerning Typhus Fever. 2. Demonstration of Rickettsiae in Mice inoculated with Endemic Mild Typhus Fever Virus.**—*Kitasato Arch. Experim. Med.* 1937. May. Vol. 14. No. 2. pp. 99–112.

ii. ——. **Experimental Studies on Mice concerning Typhus Fever. 3. Mice Passage of the Virus of the Epidemic Typhus Fever.**—*Ibid.* pp. 113–124. [14 refs.]

i. In order to infect mice with the virus of endemic typhus it is necessary to employ large doses and to inoculate intraperitoneally.

If this is done infection follows and Rickettsiae are found in all organs but are most numerous in the endothelial cells lining the peritoneal and abdominal cavities ; they are also found free in the fluid. These Rickettsiae begin to appear about the 2nd day after inoculation and are most numerous on the 4th and 5th day.

ii. Using the same technique as above 412 mice were inoculated with the epidemic virus but only in 2 could the Rickettsia be detected and only in small numbers ; it was not possible to subinoculate from these mice, in marked contrast to the behaviour of the endemic virus. The epidemic virus is difficult to establish in mice and dies out at once.

D. H.

Violle (H.). Etude expérimentale du typhus exanthématique. Sa transmission avec fièvre et exanthème chez le porc. [**Oral Transmission of Typhus to the Pig.**]—*Bull. Acad. Méd.* 1937. Dec. 28. 101st Year. 3rd Ser. Vol. 118. No. 40. pp. 809–812. With 3 figs.

A two months old pig was fed on the brain of a rat infected with endemic typhus. After an incubation period of 10 days the pig developed fever which lasted for 18 days ; blood was drawn off from the pig at the height of the fever and inoculated into two white rats, both rats developed fever and were later proved to be immune to typhus virus. Towards the end of the fever the pig developed a very definite macular rash on the flanks which became petechial. Veterinary surgeons who examined the pig said they had never before seen such a rash on a pig and agreed that it was due to the typhus infection. [A similar rash has already been described on white guineapigs infected with endemic typhus virus.] *D. H.*

Blanc (Georges) & Baltazard (Marcel). Immunité croisée entre la fièvre boutonneuse et la fièvre pourprée des Montagnes Rocheuses. Vaccination du cobaye contre ces deux maladies par un virus vivant bilié de fièvre boutonneuse. [**Crossed Immunity between Boutonneuse Fever and Rocky Mountain Spotted Fever.**]—*C. R. Acad. Sci.* 1937. Oct. 4. Vol. 205. No. 14. pp. 578–580.

Five strains of virus of boutonneuse fever and one strain of Rocky Mountain fever were employed in these experiments.

Seventy-three male guineapigs and 21 female were inoculated with the virus of boutonneuse fever ; all reacted ; when tested later with Rocky Mountain fever virus all were immune. Three Macacus monkeys were inoculated with boutonneuse virus and reacted ; when tested later with Rocky Mountain fever virus all 3 were immune, 2 controls died.

Four men who had had boutonneuse fever were first tested with large doses of the homologous virus and none reacted. They were then given large doses of Rocky Mountain fever virus. All proved to be immune.

Guineapigs were immunized with doses of bile-treated vaccine (living virus) of boutonneuse fever, there was no reaction ; later they were found to be immune to test doses of the homologous virus and also to the virus of Rocky Mountain fever. *D. H.*

VIOLLE (H.). Contribution à l'étude du typhus exanthématique murin. De la contamination du chien par ingestion du virus. [**Murine Typhus. Infection of a Dog by Mouth.**]—*Bull. Acad. Méd.* 1937. Nov. 9. 101st Year. 3rd Ser. Vol. 118. No. 33. pp. 311–315.

A young dog was fed on milk in which the brain of an infected guineapig had been emulsified. The dog had no fever and the Weil-Felix reaction was negative but samples of blood taken from the dog on the 11th, 17th and 31st day after the infective feed all proved infective for rats on intraperitoneal injection.

The author suggests that man may be infected by ingestion of food contaminated by the urine of rats. He also mentions incidentally that he has found the virus of murine typhus infective in the brains of rabbits up to 4 months after infection; he suggests that the wild rabbit may be a reservoir of this virus. He has also found that intradermal injection of small doses of virus in rats and guineapigs is useful in the rapid diagnosis of material containing typhus virus. *D. H.*

BALTEANU (I.) & CONSTANTINESCO (N.). Essais de vaccination contre le typhus exanthématique à l'aide du virus historique enrobé dans l'huile.—*Bull. Office Internat. d'Hyg. Publique.* 1937. Nov. Vol. 29. No. 11. pp. 2328–2342. With 4 figs. [16 refs.]

ALGER. **Fédération des sociétés des sciences médicales de l'Afrique du Nord. VIIe Congrès. (Alger 22, 23 et 24 mars 1937). Typhus et pseudo-typhus. Receuil des rapports, communications et conférences.**

This book was reviewed on p. 251.

PINKERTON (Henry) & HASS (George M.). **Spotted Fever. III. The Identification of *Dermacentroxenus rickettsi* and its Differentiation from Non-Pathogenic Rickettsiae in Ticks.**—*Jl. Experim. Med.* 1937. Dec. 1. Vol. 66. No. 6. pp. 729–739.

Dermacentroxenus rickettsi, the aetiological agent of the diseases of the spotted fever group, may be readily identified in infected mammalian tissues by its characteristic morphology and by its multiplication in the cytoplasm of smooth muscle cells of the blood-vessel walls. A more accurate identification of this organism can be made in mammalian tissue cultures where it proliferates in the nuclei of cells. However, non-pathogenic rickettsiae are found in the tissues of ticks which resemble in morphology *D. rickettsi*. The present research was undertaken with the view of differentiating the non-pathogenic from the pathogenic and proceeded on the following lines :—

1. What is the nature of those rickettsiae of normal ticks ?
2. How can they be distinguished from *D. rickettsi* ?
3. What is the effect on the pathogenic and non-pathogenic organisms of refeeding the ticks ?
4. If there is any such effect will this help in differentiation ?

D. variabilis ticks were collected from an area where so far as was known no spotted fever had ever occurred. Some of these ticks were dissected and injected into guineapigs. These were not affected in any way and when tested later by inoculation of spotted fever

virus all had fever and all died like the controls. Some of these ticks were embedded in paraffin and serial sections prepared and stained with Giemsa's stain: in many of these rickettsiae were found which in morphology resembled *D. rickettsi* but none was seen within nuclei of cells. Some of the female ticks were held over and, from the eggs collected from these, larvae were hatched out in the laboratory.

Eighty nymphs derived from these clean larvae were fed on normal guineapigs under elaborate and careful precautions; some were collected after feeding and dissected and injected into guineapigs, no reaction followed and no immunity was produced. Others were prepared and sectioned and carefully examined; in some of these numerous rickettsial bodies were seen throughout the tissues, although no heavy infection was seen, except that in certain cells lining isolated salivary gland acini a heavy or massive localization of the organisms was seen and necrosis of these cells was observed. Another 80 nymphs from the same batch of clean ticks were fed on infected guineapigs (spotted fever), 40 were examined microscopically and in 31 of these rickettsiae were seen in all tissues and *intranuclear localization* was noted. Six ticks showed no rickettsiae but proved infective on injection. Great variation of size of rickettsiae was noted so that on morphology alone it would be difficult to separate the pathogenic from the non-pathogenic. The only unequivocally diagnostic difference is that the pathogenic Rickettsia *D. rickettsi* is found in masses within the nucleus of infected cells. In the tick if there is massive invasion of the tissues and sparse of salivary glands, that is probably *D. rickettsi*; the non-pathogenic rickettsiae are slightly larger, are not seen in massive invasion of the tissues generally but only in certain cells of the salivary glands which become necrosed. But as already said, the only infallible differentiating point is the intranuclear multiplication. Refeeding or keeping the ticks at different temperatures or prolonged incubation had apparently no marked effect.

The authors' conclusion is that the non-pathogenic rickettsiae found in *D. variabilis* and other ticks have no well defined relationship to *Dermacentroxenus rickettsi*. *D. H.*

Bengtson (Ida A.). **Cultivation of the Rickettsiae of Rocky Mountain Spotted Fever in Vitro.**—*Public Health Rep.* 1937. Sept. 24. Vol. 52. No. 39. pp. 1329–1335. With 2 figs. & 4 plates. [11 refs.]

A modified Maitlands medium was employed in this research. The modification consisted in the use of Baker's solution in place of Tyrode's. The actual medium was prepared as follows:—

1 cc. fresh guineapig serum
4 cc. Tyrode's or Baker's solution.

The fresh tissue used was either minced chick embryo membrane or guineapig tunica. After a few tests Tyrode's solution was abandoned and Baker's used in its place as it was found that Rickettsiae were much more numerous in the latter. Living chick embryos were inoculated from infected guineapig tissue and after 4 or 5 days the membrane was removed, minced and placed in the medium in 50 cc. flasks and incubated for 10 to 70 days at 37°C. Successful subcultures were made for 14 generations.

The results are displayed in tabular form. Inoculations into animals were made from the cultures from time to time and 81 per

cent. of these animals reacted. There was no loss of virulence in the subcultures whether the inoculum was taken from the supernatant fluid or from the centrifuged deposit.

Material taken from the cultures and spread thinly over slides and stained with Giemsa stain showed numerous Rickettsiae in the cytoplasm of the cells, but not in the nuclei. *D. H.*

Bengtson (Ida A.). **Immunizing Properties of Formolized Rocky Mountain Spotted Fever Rickettsiae cultivated in Modified Maitland Media.**—*Public Health Rep.* 1937. Nov. 26. Vol. 52. No. 48. pp. 1696–1702. With 1 chart.

The vaccine was prepared from cultures in modified Maitland's solution (see above) by trituration of the inoculated tissue particles and addition of formalin in the proportion of 0·1 per cent.

Guineapigs were given 3 subcutaneous doses of 1 cc. each of the vaccine at intervals of a week and subsequently tested by doses of virulent blood : none of the vaccinated guineapigs died. The controls developed typical symptoms of spotted fever and died. *D. H.*

Dias (Emmanuel) & Martins (Amilcar Vianna). A preparação da vaccina de Spencer e Parker contra a febre maculosa das Montanhas Rochosas, no Rocky Mountain Laboratory, em Hamilton, Montana, EE. UU. [**Preparation of Vaccine for Rocky Mountain Fever.**]—*Hospital.* Rio de Janeiro. 1938. Jan. Vol. 13. No. 1. pp. 55–70. With 19 figs.

This article is very complete but, unfortunately, does not lend itself to abstraction. Those interested will be well repaid by reading the original *in toto*. The method of preparation is given with a wealth of practical detail and in turn the article deals with collection of ticks, feeding them, rearing them in quantity for producing the vaccine ; later trituration, purification, testing the protective action of the vaccine and finally its employment as a prophylactic. It is not intended for therapeutic use. There are many illustrations to describe important stages in procedure, but they are too much reduced and lack definition.

H. H. S.

Kawamura (Rinya), Ito (Tatsuji), Nakamura (Ryuji), Kamimura (Takao) & Sato (Ikuhiko). **On the Prevention of Tsutsugamushi Disease including a New Method of Fever Thèrapy.**—*Kitasato Arch. Experim. Med.* 1937. May. Vol. 14. No. 2. pp. 75–98. With 13 charts.

Strains of the virus of tsutsugamushi fever vary greatly in virulence—the fever in Japan is severe and often fatal, whereas in the Pescadores the disease is a mild one.

The authors therefore suggested that this mild virus might be employed in fever therapy of nervous diseases just as malaria is used.

One cc. of the emulsion of the testicle of a rabbit, which was infected with the Pescadores strain was inoculated into each patient ; 22 cases in all were treated, 18 of these showed a reaction, the symptoms were mild, slight headache and fever, none of the patients had to take to bed.

Eight days after the fever due to the mild virus had ceased 20 patients were inoculated with the potent Japanese virus, slight fever developed in 4 cases, in 16 there was no fever and no rash. Slight improvement was noted in the condition of the mental patients.

D. H.

OROYA FEVER AND VERRUGA PERUVIANA.

PINKERTON (Henry); WEINMAN (David); HERTIG (Marshall). **Carrion's Disease. I. Behavior of the Etiological Agent within Cells growing or Surviving** *in vitro* [PINKERTON & WEINMAN].—*Proc. Soc. Experim. Biol. & Med.* 1937. Dec. Vol. 37. No. 3. pp. 587–590. With 2 figs. **II. Comparative Morphology of the Etiological Agent in Oroya Fever and Verruga Peruana** [PINKERTON & WEINMAN].—*Ibid.* pp. 591–593. With 1 fig. **III. Experimental Production in Animals** [WEINMAN & PINKERTON].—*Ibid.* pp. 594–595. **IV. Natural Sources of Bartonella in the Endemic Zone** [WEINMAN & PINKERTON].—*Ibid.* pp. 596–598. **V. Studies on Phlebotomus as the Possible Vector** [HERTIG].—*Ibid.* pp. 598–600.

These papers summarize observations made by the Harvard 1937 Expedition to Peru organized by Dr. Richard P. STRONG.

I. Tissue cultures were prepared in modified Maitland cultures; these cultures were inoculated with one or two drops of material from the following sources:—

1. Blood from a severe case of Oroya fever.
2. Cultures in leptospira-medium which showed Bartonella made from the blood of 7 cases of fever.
3. Similar cultures from lymph nodes and bone marrow of the same cases.
4. Cultures in leptospira-medium from the blood and from cutaneous nodules of cases of verruga.
5. Cultures from the blood of monkeys inoculated from cases of Oroya fever and verruga.

In tissue cultures of both types, that is, Oroya fever or verruga, infected from all 5 sources, bartonella were found in abundance, often free but always multiplying voluminously in the cytoplasm of the tissue cells. In early cultures small clusters of diplobacillary rods were seen in the cells. Later many cells were packed with such clusters of organisms; this characteristic pattern of cell invasion was found in the tissue cultures from all 5 sources. Cell nuclei were not invaded. This peculiar pattern of cell infection could be readily distinguished from that of typhus rickettsiae although individual bartonellae could not be easily distinguished from typhus rickettsiae. The results of these experiments provide further evidence that Oroya fever and verruga are manifestations of one and the same disease and that the parasites causing these conditions are the same.

II. Tissue removed from 3 fatal cases of Oroya fever and cutaneous nodules from 7 cases of verruga peruviana were examined. Bartonella-filled cells were found in large numbers in nearly all organs of human Oroya fever cases, in cutaneous nodules from afebrile and non-anaemic

cases of verruga and also in cutaneous nodules produced in monkeys by inoculation with human material from Oroya fever and verruga. The morphological identity of the organisms and the essential identity of the patterns produced by them within the cells in all of the above tissues furnish additional evidence that Oroya fever and verruga have a common etiological agent, *Bartonella bacilliformis*.

III. The 3 types of Carrion's disease seen in human cases, the cutaneous form, the anaemic form and the asymptomatic form were all reproduced in monkeys. The cutaneous form was produced by the inoculation of (*a*) infected lymph nodes from a patient with the anaemic form (Oroya fever), (*b*) human verruga tissue, (*c*) cultures of Bartonella from the blood of human verruga cases. The anaemic form (Oroya fever) was reproduced in one splenectomized monkey by the inoculation of blood from an Oroya fever patient. This animal died and showed a multiple infection of his red cells with *B. bacilliformis*.

The asymptomatic form was produced in monkeys by the inoculation of blood from Oroya fever patients.

IV. Healthy inhabitants of a village in the verruga zone were discovered to be asymptomatic carriers of *B. bacilliformis*. Five of these yielded positive blood cultures, 3 had no history of any illness, 2 had had verruga some time previously.

V. Sandflies *Phlebotomus verrucarum* and *P. noguchii* were fed on patients showing many bartonellae in blood films; these flies became infected with a bartonella-like organism not as yet identified. A similar infection was found in only one of the many wild sandflies examined. Transmission experiments, limited in number, with sandflies and monkeys resulted negatively so far. *D. Harvey.*

DENGUE AND SANDFLY FEVER.

Coles (Alfred C.). **A Microscopical Inquiry into the Aetiology of Dengue, Sandfly, and Yellow Fever.**—*Jl. Trop. Med. & Hyg.* 1937. Sept. 15. Vol. 40. No. 18. pp. 209–214. With 4 figs. [14 refs.]

The author has been able to find in Giemsa-stained blood films from cases of dengue fever in man, yellow fever in monkeys (first three or four days) and sandfly fever in man (first 24 hours) granules which are within the red blood corpuscles or free in the plasma, which he regards as the causal organisms of these diseases. Though many of the granules are evidently too large to be filter passers, some are sufficiently small to be of this nature. They are to be found in the blood only during those periods of the disease in which the blood is actively infective on inoculation. The paper describes in detail the technique used by the author and gives his reasons for the conclusions he has reached. *C. M. Wenyon.*

Karamchandani (P. V.). **Study of 110 Cases of Dengue Fever in the Madras Penitentiary.**—*Indian Med. Gaz.* 1937. Sept. Vol. 72. No. 9. pp. 532–534. With 28 charts.

One hundred and ten cases of dengue fever occurred in the Madras Pentitentiary. There was sudden onset of the fever with intense

headache and backache, slow pulse and leucopenia. A terminal eruption was not noted in any of the cases but in one European case a typical dengue rash developed. Fifty-four of the cases showed the saddle back type of temperature chart. Seventeen showed a continuous fever lasting about 6 to 7 days and 39 cases had fever for 3 to 4 days only without any secondary rise. Of 3,000 mosquitoes captured in the jail only 3 were *Aëdes*, the remainder were *Culex* and were mostly gorged females. The author suggests that *Culex* may be the vector in this instance, but gives no further proof. The editor, in a footnote, is "not convinced." *D. Harvey.*

Melissinos (Johann). Pathologisch-anatomische Untersuchungen bei Denguefieber. [**Pathology of Dengue.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1937. Mar. Vol. 41. No. 3. pp. 321–331.

Three cases are reported in detail, these were some of the fatal cases met with in the big epidemic in Athens in 1930. The types of pathological changes seen were inflammatory, haemorrhagic and oedematous. It is also suggested that in dengue fever, as in smallpox, measles and influenza, there may be a form of encephalitis. *D. H.*

Le Gac (P.). Etude de la bradycardie au cours de la fièvre à pappataci. [**Bradycardia in Pappataci Fever.**]—*Bull. Soc. Path. Exot.* 1937. July 7. Vol. 30. No. 7. pp. 536–539. With 3 figs.

According to the author bradycardia is a constant symptom of sandfly fever, but is not met with until the second day of the fever and is accompanied by severe headache. This slow pulse rate is due to a hypertension of the cerebrospinal fluid and is relieved by lumbar puncture. In some cases the pulse rate may be as low as 40 per minute and the pulse rate remains low in some cases for several days after the fever has ceased. *D. H.*

Sellar Fever.

Jack (W. A. M.). **Sellar Fever.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1937. Nov. 30. Vol. 31. No. 3. pp. 281–296. With 5 charts.

Definition.—A mild fever showing a saddle-back (hence the name) temperature chart and lasting in the typical form for 5 days, but which may have a duration of any period from 12 hours to 6 or more days. It is accompanied by frontal headache, congestion of the throat and a slow pulse and there is a special liability to relapse. The author has carried out investigations into this disease among Indian troops for many years and in many stations in northern India: he has personally observed more than 1,000 cases. The principal investigations took place in Razmak in 1932, Ambala in 1933 and in Sialkot from 1934 to 1937. In Sialkot in 1936 over 500 cases occurred in a garrison strength of Indian troops of 2,000.

A careful clinical description of cases is given in detail; the incubation period is difficult to determine but lies between 5 and 20 days; the onset is sudden and accompanied by shivering as a rule. Frontal headache and a sense of fever are invariably present; sore throat is

noted in 75 per cent. of cases; there may be backache and general pains. The course of the fever usually lasts 5 days, but may be anything from 12 hours to 6 or more days, and may occasionally be prolonged by relapse or relapses. The temperature may reach 104° or may be only slightly above normal. In 2 per cent. of the cases an early erythematous rash was noted on the first day, but later rashes were not seen. Apart from some enlargement of the glands draining the pharynx no enlarged glands were noted. A leucopenia occurs with relative increase of lymphocytes at the expense of polynuclear cells and eosinophiles. Of 411 cases observed in 1934 to 1936, 53 relapsed, or 12·9 per cent.; these relapses usually begin on the 6th day, there may be more than one relapse, as many as six have been noted in one case. Bronchitis is the only complication noted. A striking feature of the disease is the mildness of discomfort and even when the temperature is high and fever prolonged there is no toxaemia and the general appearance of the patient is good and convalescence is rapid.

The saddle-back type of the temperature chart is caused by a distinct drop in the earlier part, perhaps to normal limits, which divides the course into 2 periods; this remission usually commences either on the second or third morning, but may commence on the first evening. Typical temperature charts are given of cases with fever of 1, 2 and 3 days duration, 4 days duration and 5 and 6 days duration.

Diagnosis.—The throat condition is a symptom of the disease and not the cause of the fever; there is no true tonsillitis and no catarrh.

As regards the differential diagnosis from dengue, sandfly fever and influenza, diseases with which sellar fever is most readily confused, this disease occurs frequently in the cold weather in Razmak at an elevation of over 6,000 feet when deep snow lies on the ground and there are no *Aëdes* mosquitoes or other winged insects. Dengue never occurs under such conditions. There are no late rashes in sellar fever and no "break bone" pains or joint pains and no injection of the conjunctiva; the remission of temperature occurs 24 hours before that in dengue fever and the disease lasts much longer than sandfly fever and occurs in places where neither phlebotomus nor sandfly fever are met with.

The aetiology is still in doubt but an insect vector is probable. Lice are excluded as careful lousing of units had no effect on the incidence and attempts to transmit the disease by means of lice failed. The bed-bug is a possible vector. Bed-bugs were fed on patients and later fed on volunteers, two of these developed fever, but as cases were occurring at the time natural infection could not be ruled out and later attempts failed. The disease is definitely not spread by food, milk or water and does not spread in hospital to other patients or attendants. Blood taken from a patient and injected into a volunteer had no effect nor had swabs from the throats of patients. The disease is endemic throughout the year; sporadic cases occur in the barrack rooms, then more and more cases in one barrack resulting in a series of minor epidemics. Many cases may occur in a barrack room and other companies of the same regiment camped within a short distance may have only one or two cases, although the food and water are the same for all. British officers of units are rarely infected and if they are the disease does not spread to their families.

Conclusions.—A very large number of cases of mild fever characterized by a saddle-back temperature, frontal headache, slow pulse and sore throat have been observed in various stations in Northern India. The clinical features suggest a resemblance to the

sandfly-dengue group, but there are many definite differences. The disease has a distinct tendency to relapse and it is these relapses which form a large proportion of the otherwise undiagnosed fevers common amongst Indians in the North of India. The existence of an insect vector, perhaps the bed-bug, is possible.

There can be no doubt that this is a disease *sui generis* hitherto undescribed and to it the name "sellar fever" is now given, in allusion to the typical course of the fever. [This name might give rise to confusion as dengue is also a "sellar fever."] *D. H.*

HELMINTHIASIS.

i. Chandler (Asa C.). **Studies on the Nature of Immunity to Intestinal Helminths. V. Experiments on the Rôle of the Skin in Parenteral Immunity, and Further Experiments on Passive Immunization in Nippostrongylus Infections in Rats.**—*Amer. Jl. Hyg.* 1937. Sept. Vol. 26. No. 2. pp. 292–308. With 1 fig. [10 refs.]

ii ——. **Studies on the Nature of Immunity to Intestinal Helminths. VI. General Résumé and Discussion.**—*Ibid.* pp. 309–321. [32 refs.]

i. "1. Experiments are described which indicate that rats previously infected with Nippostrongylus by skin penetration allow as many larvae to reach the intestine as do rats previously infected by subcutaneous injection or by intestinal implantation, whether the test infections are given through or under the skin. More larvae are found in the intestines of uninfected controls due to the failure of many larvae to establish themselves in the intestine after reaching it in rats already harbouring intestinal worms.

"2. Histological methods failed to demonstrate increased retention of larvae in skin previously exposed to penetration by Nippostrongylus, although leukocytic infiltration and eosinophilia were enhanced.

"3. Immunization with live *Ancylostoma caninum* larvae afforded no immunity to Nippostrongylus. Rats repeatedly infected with *A. caninum* by skin penetration showed less skin reaction to a heavy penetration by this worm than did rats repeatedly infected by subcutaneous injection.

"4. Rats immunized to *A. caninum* failed to show any enhancement of skin reaction to penetration by Nippostrongylus larvae, thus proving the heightened skin reaction to be spécific.

"5. Rats treated with 6 cc. per 100 gm. of serum from rats highly immunized by repeated skin penetrations by Nippostrongylus showed no effect on the successful migration of larvae to the intestine but showed evidence of a slight effect on establishment of worms in the intestine and on egg production. (The rats were not Bartonella-free.)

"6. Rats treated with 6 cc. per 100 gm. of serum from rats immunized by repeated implantation of worms into the intestine failed to show any effect whatever on successful migration to the intestine, on establishment in the intestine, or in egg production."

ii. A summary of the conclusions drawn from the five papers which have already been abstracted or noticed by title (this *Bulletin*, 1936, Vol. 33, p. 120, 588; 1937, Vol. 34, p. 39). *Clayton Lane.*

Vazquez Pausa (Antonio). Tratamiento de la tricocefalosis por el citrato de hierro y amonio a altas dosis. [**Trichuris Infestation; its Treatment by Citrate of Iron and Ammonium.**]—*Archivos Med. Infantil.* 1937. Oct.–Nov.–Dec. Vol. 6. No. 4. pp. 469–470.

Ferri et ammonii citras given at first with a view to combating secondary anaemia was found, to the author's surprise, to be followed by rapid disappearance of the ova of *Trichuris trichiura* from the faeces, within 10 days, if large doses, 4–5 gm. daily, of the drug were

administered. In 1935 he studied the question more thoroughly, and has now observed about 300 patients so treated. His prescription is :—

Ferri et ammon. cit.	20·00
Manganes. cit.	0·40
Cupri cit.	0·10
Vinum de Málaga vel Elix. simpl.	300·00

He concludes :—

1. Ninety per cent. of cases are cured in 10–15 days.
2. As a rule the limit of tolerance is 4 to 6 gm. daily, but some can take up to 12 gm., the only untoward symptom being diarrhoea, which ceases when the dose is reduced.
3. There is no need for the patient to go on any special diet.
4. It benefits the associated anaemia, raising the number of red cells and the haemoglobin content.
5. It is cheap and therefore specially recommends itself for the poor who are the chief sufferers from this form of helminthic infestation.
6. The drug can be put up in "effervescing pastilles" each containing one gram of the drug ; this is dissolved in a cup of sweetened water and is well taken by children. *H. H. S.*

Wright (Willard H.), Bozicevich (John) & Gordon (Leon S.). **Studies on Oxyuriasis. V. Therapy with Single Doses of Tetrachlorethylene.**—*Jl. Amer. Med. Assoc.* 1937. Aug. 21. Vol. 109. No. 8. pp. 570–573.

The studies II, III and IV are still unpublished. For Study I see this *Bulletin*, 1937, Vol. 34, p. 878.

"In experiments reported in this paper, forty-seven boys infested with pinworms were treated with single doses of tetrachlorethylene administered orally at the rate of 0·1 cc. for each year of apparent age. The administration of this drug in a solution of magnesium sulfate provoked disagreeable reactions in a considerable percentage of twenty-five cases, but these reactions were largely obviated by the substitution of magnesium citrate as a purgative in the remaining cases.

"Of forty-four infested boys who received tetrachlorethylene orally and were checked by post-treatment swab examinations on approximately the fourteenth and twenty-first days after treatment, thirty, or 68·2 per cent., were negative, but the true percentage of cures is probably about 47·7 per cent. as arrived at after the application of a correction figure of 30 per cent. for positive cases not disclosed by two swab examinations.

"Three boys received magnesium citrate solution alone, followed the next morning by an enema consisting of 1 cc. of tetrachlorethylene in a coconut oil soap emulsion to 1 liter of water. These three boys were negative on post-treatment swab examinations, but in no case did the magnesium citrate solution remove all worms.

"The number of worms recovered from individuals in these tests varied between 1 and 4,958 ; the average infestation was 255·8 worms.

"Evidence indicated that tetrachlorethylene administered orally in single doses was more effective in eradicating relatively light pinworm infestations than it was in eradicating relatively heavy infestations, since only two of our thirty negative cases treated in this manner showed infestations above the mean.

"So far as there is available evidence, it would appear that tetrachlorethylene is one of the best drugs for a single-dose treatment for pinworms. It is especially effective, apparently, for light pinworm infestations, but

will probably fail to effect cures in the majority of persons heavily infested with pinworms, a failure which would probably be shared by other anthelmintics of merit when similarly administered."

C. L.

Cram (Eloise B.), Jones (Myrna F.), Reardon (Lucy) & Nolan (Mabelle O.). **Studies on Oxyuriasis. VI. The Incidence of Oxyuriasis in 1,272 Persons in Washington, D.C., with Notes on Diagnosis.**—*Public Health Rep.* 1937. Oct. 22. Vol. 52. No. 43. pp. 1480–1504. [39 refs.]

" The evidence indicates that pinworms are much more prevalent than is generally believed, that the usual methods employed in diagnostic laboratories and in the majority of surveys, namely, faecal examination for eggs, is not reliable for their detection, and that examinations by a method such as the use of the NIH swab should be repeated several times before a negative diagnosis is justified."

Of the 1,272 examined, 628 came from the general population, were mostly of low social-economic level, the examinations were often made because of clinical symptoms or because other members of the family had been found positive ; while 644 were (apart from 27 girls) boys aged from 11 to 19 in institutions. For those from the general population, the N.I.H. Cellophane scraper was used ; of boys in institutions, 400 who were already inhabitants of these institutions were examined by various swabs and scrapers before the Cellophane scraper was fully established, and thereafter 217 boys were examined by Cellophane scraper at the time of admission.

Of the 628 persons from the general population, 406 were negative, the number of scrapings being 1 to 14, though 87·3 per cent. had not more than two ; the sexes were about equal, and 82·8 per cent. were under 19 years old. Of the 222 positives the percentage of infected among 476 white persons was 41·2 and among 90 coloured persons 21·1 ; the highest percentages were in those from 6 to 18 years of age ; the need for repeated examination is shown by the fact that the percentages of the 222 which were found positive in 1 to 6 examinations were respectively 80·7, 93·7, 98·2, 99·1, 99·5, 100 ; by such repetition of examination the percentage of positives was raised by from 28·5 to 35·4.

Of the 617 boys in institutions, the percentage of infection in the 400 who were already living in them and who had been examined by swabs of various kinds was 3·7, in 217 newly admitted and examined by the Cellophane scraper it was 7·8. The uselessness of faecal examinations in the detection of this infection is further shown by the fact that they were made (the method is unstated) in 42 persons known to be infected, and there were eggs in 4, or 9·5 per cent. only.

C. L.

Nicolesco (P.), Strat (C.) & Iamandi. Diagnostic étiologique de la septicémie trichinosique. [**Trichinous Septicaemia Diagnosed by the Disclosure of its Causal Organism.**]—*Bull. Acad. Méd. Roumanie.* 1937. Vol. 4. No. 5. pp. 585–589.

The paper urges the wisdom of blood examination for larvae of trichinella in any early case of suspected trichinosis fever.

They note work by Busse of Posen, who found at autopsy of persons over 60 years of age trichinae in the muscles of 18 per cent. and who holds that the cooking habits of Germans easily explains this high incidence, which he says exceeds that of American countries. In Rumania, infection cannot be combated effectively, since peasants will not take their beasts to veterinary surgeons, nor have autopsies been used to check the incidence in man. Eosinophilia and the finding of larvae in the faeces are uncertain in diagnosis for different reasons. Biopsy is difficult, and it is late before it is of use for diagnosis, moreover in Rumania it has been refused more often than not. By examination of blood for embryos, seven cases were investigated, 4 in one family, 2 in another, the third being solitary; larvae were found in the blood in 2 on the seventh and twelfth days respectively. The method used was that of Stäubli; 10 cc. of blood were laked in a 100 cc. of a 30 per cent. solution of acetic acid and the centrifuged precipitate examined. In one case this deposit from 20 cc. of blood was spread over 40 to 50 slides and there were found two complete and some partially destroyed embryos. In the case examined on the 12th day when the temperature was 37·5 there were found some embryos damaged by centrifuging. This method is advised as easy to put through and within the capacity of every practitioner. *C. L.*

Sawitz (Willi). **Are Post-Mortem Statistics on Trichinosis Valid for the Living Population ?**—*Amer. Jl. Public Health.* 1937. Oct. Vol. 27. No. 10. pp. 1023–1024.

The answer to the question in the title is, Yes—so far as the relatively small numbers examined are evidential.

Sawitz made 200 autopsies and 200 examinations by skin test. In the autopsies on 200 bodies from the Truro Infirmary and the Charity Hospital, New Orleans, the examination for measles was by artificial gastric digestion of 50 gm. of diaphragm and 10 gm. of pectoral muscle in each case. The intradermal skin test was made on patients of the Truro Infirmary and Hutchinson Memorial Clinic of the Tulane Medical School. The antigen for the skin test was 0·1 cc. of a 1 in 5,000 solution of dried and powdered trichinella larvae in Coca's solution injected intradermally the result being read after 15 minutes. The results gave a 5 per cent. infection both in the dead and in the living. Of those tested for skin reaction 43 were negroes. The absence of a reaction in them "was probably due to the difficulty of seeing the reaction on coloured skins." If so, infection in the living is greater than the autopsy tests indicate. Apart from that exception, the figures by sex, race and age are, it is noted, remarkably near. No person in either series had given a clinical history of trichinosis.

	No. Cases Examined	Positive	Percent. Positive	Percentage Distribution by							
				Sex		Race		Age in Years			
				M.	F.	W.	C.	0–19	20–39	40–59	60–79
Autopsies ...	200	10	5	5·8	3·7	7·1	3·4	0·0	3·3	4·9	10·0
Living Persons	200	10	5	7·1	3·8	6·3	0·0	0·0	3·8	5·3	15·7

C. L.

Joses (Maurice) & Wells (John J.). **Trichinosis. A Report of Two Cases.**—*U.S. Nav. Med. Bull.* 1937. Oct. Vol. 35. No. 4. pp. 475–480.

In one of these two cases the diagnosis was certain, for measles were found in a piece excised from the left gastrocnemius, in the other it was inferential.

The case histories are given in detail. There was the usual puffiness of the lids and tenderness of muscles with eosinophilia in both men. He in whom trichinae were found in the muscle had a positive precipitin reaction in a dilution of 1 in 1,600, and had " skin test positive " ; and 5 days before his illness began he had bought, had himself imperfectly cooked, and had eaten sausage meat. The other man had a history of eating cooked pork sausage ; a piece of excised gastrocnemius showed no trichinae, " skin test mildly positive ; precipitin test doubtful." *C. L.*

Pierce (G. N.), Jr. & McNaught (James B.). **Effects of Alcohol on *Trichinella spiralis*.**—*Proc. Soc. Experim. Biol. & Med.* 1937. June. Vol. 36. No. 5. pp. 579–581.

" We conclude that a concentration of 25 per cent. alcohol has little direct action on trichinella [larvae] *in vitro* but that concentrations as low as 9 per cent. interfere with the digestive liberation of encysted trichinella."

The liberal use of alcohol has been advised, with meat which may be trichinous, as a means of preventing infection from its ingestion. To test the point two sorts of *in vitro* experiments were put through. In the first 5 grams from a quantity of ground up and thoroughly mixed trichinous rat meat and 100 cc. of artificial gastric juice were put into each of 6 beakers, and to each beaker certain additions were made ; namely, to No. 1 water 10 cc., to No. 4 ethyl alcohol 10 cc. ; to No. 2 water 20 cc., to No. 5 ethyl alcohol 20 cc. ; to No. 3 water 30 cc., to No. 6 ethyl alcohol 30 cc. From the controls, that is Nos. 1, 2 and 3, all the larvae recovered were free and alive, and their numbers were 13,150, 13,550 and 11,500 respectively ; from Nos. 4, 5 and 6 none of the recovered larvae were active, the recoveries from No. 4 were 7,660 dead, from No. 5 were 400 capsulated and 3,600 dead (total 4,000), and from No. 6 were 790 capsulated and 1,860 dead (total 2,650). Alcohol then increasingly interfered with the liberation of the larvae by digestion. In the second set of experiments 1,000 larvae freed by gastric digestion were added to 2 cc. of ethyl alcohol in different dilutions, so that its strength varied from 25 to 0·1 per cent. After being at body temperature for 6 hours all larvae were held to be still living in all strengths of alcohol, that is they were active or tightly coiled, and were not comma shaped. After 12 hours at body temperature all those in 25 per cent. alcohol were dead, after 24 hours all in 6·25 per cent. were dead, after 48 hours all in 1·5 per cent. were dead and at least half of those in lower dilutions. In the human stomach a strength of even 6·25 per cent. is not maintained for these long periods. *C. L.*

Wantland (W. W.). **Blood Studies on Normal and Trichinized White Rabbits.**—*Jl. Lab. & Clin. Med.* 1937. Oct. Vol. 23. No. 1. pp. 32–38. With 1 chart. [11 refs.]

" Blood studies on a series of twelve trichinized rabbits revealed that a polycythemia occurring as early as the second week after infection,

closely paralleled by an increase in hemoglobin percentage and a rise in specific gravity, occurred in seven of the twelve animals following infection with *Trichinella spiralis*.

" Hypereosinophilia was definitely associated with marked symptoms of trichiniasis. A noticeable decrease in clotting time, three to five weeks following infection, and a definite erythrocytic macrocytosis (observed in most cases less than three weeks after infection) seemed indicative of trichina infection in the white rabbit.

" The production of toxins in the intestinal, blood and muscle phases of the disease very probably is one of the main factors concerned in the disturbance of the normal blood picture." *C. L.*

i. Hinman (E. Harold). **Filarial Periodicity.**—*Jl. Trop. Med. & Hyg.* 1937. Sept. 1. Vol. 40. No. 17. pp. 200–205. With 1 chart. [21 refs.]

ii. Lane (Clayton). **Filarial Periodicity.**—*Ibid.* Nov. 1. No. 21. pp. 262–263.

i. " The problem of the mechanism of filarial periodicity is far from settled. In the case of *Dirofilaria immitis* the evidence points strongest to a continuous larval production, but in *Wuchereria bancrofti* the experimental evidence must be considered inconclusive."

After pointing out Manson's statement regarding microfilariae in the blood " In the dog there is during the day a remission in numbers, in man an intermission," Hinman adds, " It seems evident that if a factor controlling periodicity can be determined in the filariae of the dog, then an important lead may be produced for studies on the human infection." After noting Lane's papers favouring the view that in *W. bancrofti* there is simultaneously timed parturition of female worms and O'Connor's evidence in its support he adds :—

" Such a condition would explain filarial periodicity provided that, first, a comparable destruction of microfilariae occurs shortly after midnight, and second, that the female worms are capable of producing daily sufficient numbers of embryos to account for the enormous counts seen in many cases. To date there seems to be no evidence on this first proviso but the writer has information on the second matter concerning *Dirofilaria immitis* and this will be discussed below."

The paper goes on to consider the second proviso. Taking microfilarial counts in 20 cmm. of blood, estimating the quantity of blood as one-twelfth of the body weight, killing the dogs, and counting the female worms in the heart and great vessels, there was no correlation at all between the numbers of these and of larvae, the variation being from 10,740 to 3,750,945 per female worm.

" If cyclical parturition is responsible for periodicity in the dog heart-worm, then 50 per cent. of the maximum number must be produced anew each day and a corresponding number be destroyed every twenty-four hours. That a single female *Dirofilaria* could daily produce even half of the above-mentioned numbers seems incredulous."

There is then cited an experiment by Knott [referred to as No. 6 in Lane's paper already quoted] as the most conclusive evidence against the short life of human microfilariae. " Certainly if the embryos can survive up to two weeks following transfusion they probably do live much longer in their original host. What happens to over 90 per cent. of the microfilariae immediately following transfusion remains a mystery." Then are described 12 of 62 experiments in which fertilized female dirofilariae were kept *in vitro* in saline or

Ringer's solution at 39°C., 0·1 cc. of the fluid being removed at intervals for a microfilarial count.

"In practically every instance the greatest numbers of microfilariae have been produced within the first six to twelve hours after introduction of the female worms into the media. This has occurred irrespective of whether the animal was sacrificed at 7 a.m. or 7 p.m. In general, the graph shows a marked diminution in numbers or complete cessation of microfilariae produced after a period of twelve or more hours. This may be due to the fact that the worms were present in somewhat abnormal conditions and seldom lived beyond thirty-six hours. The individual worms showed marked variation in the numbers of microfilariae produced, both in the first six to twelve-hour period and in the total number produced in twenty-four hours. The maximum number produced was slightly in excess of 20,000 in twenty-four hours (in an experiment not included in the Chart). The majority of the worms produced between 4,000 and 10,000 microfilariae during the twenty-four-hour interval.

"The writer is well aware of the fact that no definite conclusions can be drawn from the above-cited experiments. However, it is believed that if female *Dirofilaria* undergo cyclical parturition in their normal habitat, there should have been some indication observable in the above experiments. All of the data obtained point to a more or less continuous parturition being carried on by this species. It would be most interesting to carry on similar experiments with *Wuchereria bancrofti* in those hospitals where the female worms may be secured in surgical specimens."

"The matter of visceral concentration of microfilariae, especially in the pulmonary vessels, was demonstrated by Manson in 1883 in the dog and has been confirmed by others, including Fülleborn (1908). No satisfactory explanation has been offered concerning this occurrence and its exact relation to periodicity remains unknown. In *Dirofilaria* the parent worms are located in the right heart and thus the pulmonary circulation provides the first filter for the microfilariae." [It of course equally does so for *Mf. bancrofti* which enters the blood at the great systemic veins at the root of the neck.]

ii. Lane points out that some of Hinman's doubts had already been anticipated in a paper [this *Bulletin*, 1937, Vol. 34, p. 885] which had not reached Hinman before his had left his hands. But he considers again the case "which Hinman feels to be the most conclusive evidence against the belief that microfilariae are short lived in the body of man." He points out that absence of microfilariae in the blood is no proof whatever of absence of infection with *Wuchereria bancrofti*. He instances this by the experience of Bahr in Fiji (1912) when puncture of a lymph node produced eggs, microfilariae and their sheaths, yet no microfilariae were found in the blood till eight months later. Their absence from the blood being no evidence of absence of infection, this can be insured only by the choice, for experiment, of someone who has spent all his life in a non-endemic area. The man used by Knott had not done so and indeed when re-examined later he had large pendant hydroceles.

"Accordingly it is quite inadmissible to assume that he was free from this infection at the time when microfilariae were injected into his blood-vessels. It is at least as likely an explanation of what happened, as is the one which Hinman puts forward, to say that before the injection the parts of the reticulo-endothelial system concerned were able to keep back, from flooding the blood-stream in appreciable numbers, the microfilariae which were being daily posited by mother worms; but that the cells in question were overwhelmed and the system blocked when 700,000 additional microfilariae were suddenly injected into the blood-stream—it being kept in mind that microfilariae may be brought to these cells equally by the

blood and the lymph-currents. If the latter explanation is the true one the condition seems to be that which would be found if female worms living in this man were periodically positing microfilariae, if these had before the injection the short life which I believe to be normally forced on them by the mobile reticulo-endothelial cells, if this system became blocked by the sudden injection into the man's blood of 700,000 additional microfilariae, and if it later recovered from the blockage and again became able to prevent periodically posited microfilariae from reaching and flooding the blood-stream. Although put here in the form of suppositions, these are in reality steps in a line of argument for which evidence has been put forward in my cited paper. To sum up, there may not be made, so I see it, the assumption that the microfilariae seen in this man's blood for fourteen days after the injection were those that had been injected ; it is at least as reasonable to consider them as being others posited periodically and daily, by female worms already harboured by the man, and now able to reach his blood."

He urges further examinations and adds that before Professor O'Connor's death he had received from him sections from yet more persons showing destruction by the reticulo-endothelial system of microfilariae which had got into the blood. *C. L.*

Galliard (Henri). Recherches sur l'importance actuelle de la filariose humaine au Tonkin. [**The Real Importance of Filariasis in Man in Tonking.**]—*Bull. Soc. Méd. Chirurg. Indochine.* 1937. June–July. Vol. 15. No. 6. pp. 642–645.

Local filarial infection is considerable, but clinical manifestations rare.

Galliard compares the percentages of microfilariae in smears got by Mathis and Leger in 1911 and by himself in the same areas in 1937. His own are much higher. For all the Delta provinces the 1911 figures were 1,794 examined with a percentage of infection of 4·98, his corresponding figures for 1937 being 1,121 and 7·2 ; in the middle region the figures of examined and infected were, in 1911, 2,740 and 3·8, and in 1937, 1,363 and 7·27. In the high country these figures were 604 and 1·65, and 241 and 3·7. It is believed that this is not proof of an increase in infection in 26 years, but is the effect of the mode of examination—three thick drops now as against smears in 1911 ; nor is it believed that the new figures really show the extent of infection since on occasion a single microfilaria only has been found in the 3 thick drops. *C. L.*

Hu (Stephen M. K.), Wong (Helena) & Li (Bi Cu). **A Brief Survey of Filariasis in Foochow and Futsing Regions, South China.**—*Chinese Med. Jl.* 1937. Oct. Vol. 52. No. 4. pp. 571–578. With 1 map.

The survey covers blood examinations of 500 persons in Foochow, and of 266 in Futsing City. In Foochow the blood was taken between 10 p.m. and midnight. For Futsing the same appears to hold.

The 500 persons in Foochow were made up of 367 in-patients in the Foochow Union Christian Hospital, 102 members of the hospital staff, and 31 hospital servants. The infected numbered 28, 24 harbouring *Mf. bancrofti* and 4 *Mf. malayi*. These last had never been

outside Fukien Province. The examinations in Futsing followed on the discovery of elephantiasis when R. C. ROBERTSON was investigating schistosomiasis there. Of the 266 examined 151 were patients and members of the staff of the Lucie F. Harrison Hospital, students of two middle schools, and servants of these institutions ; while 115 were prisoners. There were infected with *W. bancrofti*, 12 of the 151 (7·9 per cent.) and 26 of the 115 (22·6 per cent.). In one house there lived a man whose blood had 62 embryos in a thick film taken about 11 p.m. His mother too had embryos in the blood, his wife and his daughter, aged 12, had none. A week's collection made in that house, each morning, secured 15 *Culex fatigans*, but it is noted that the door was kept open at night ; of these culex 5 were infected, the larvae in 2 being still long and narrow, in 1 sausage shaped and in 2 in the infective stage. Moreover, in Lungtien there were 18 known cases of elephantiasis in a population of about 5,000 ; and 3 of 40 persons (7·5 per cent.), mostly patients and nurses at the Woolsten Memorial Hospital, were infected with *W. bancrofti*. *C. L.*

LIU (Kusum). **Filariasis in Changsha. Preliminary Report.**—*Chinese Med. Jl.* 1937. Oct. Vol. 52. No. 4. pp. 579–582.

The parasite seen was *Mf. malayi*.

Changsha, the capital of Hunan, has a population of about 300,000, a mean minimum temperature of 20°C. or over for 5 months of the year and a mean relative humidity between 64·9 and 81·7. Examination was made of the centrifuged precipitate of about 1 cc. of blood after the latter had been mixed with 5 cc. of 2 per cent. acetic acid. It was examined first unstained, and then dried and stained with methylene blue if there were microfilariae in it. The persons examined numbered 80, of whom 79 were unselected in-patients and 1 an attendant ; 59 were males and 21 females. In this night blood *Mf. malayi* was found twice, once in a male and once in a female, neither of whom had symptoms or signs of any kind. After the report was written the same parasite was found in a man who had elephantiasis of the scrotum. All persons were inhabitants of Hunan. The microfilariae were identified by L. C. FENG. *C. L.*

GALLIARD (H.). Distribution géographique de *Filaria malayi* et de *Filaria bancrofti* au Tonkin. [**Geographical Distribution of *F. malayi* and *F. bancrofti* in Tonking.**]—*Bull. Soc. Path. Exot.* 1937. July 7. Vol. 30. No. 7. pp. 573–577. [16 refs.]

In Tonking *Mf. malayi* is about twice as common in the blood of filarial subjects as is *Mf. bancrofti*.

Of 1,613 persons examined, *Mf. malayi* was found in 62 and *Mf. bancrofti* in 37. The percentages in different regions differed markedly, being respectively 5·2 and 2·2 among 1,121 cases from the delta, 1·2 and 1·6 among 251 from the middle region, and 0·41 and 3·3 among 241 from the high region, *Mf. malayi* being practically absent about Hanoi. The point is stressed that in elephantiasis of the lower limbs, *Mf. malayi* was present in 20 per cent., while *W. bancrofti* was always the only cause of urinogenital lesions. *C. L.*

TANAKA (Shigeo). **Investigations and Clinical Observations on Microfilaria among Formosan Chinese in Boko Island.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1937. Aug. Vol. 36. No. 8 (389). [In Japanese pp. 1815–1824. With 4 figs. on 1 plate. [21 refs.] English summary p. 1825.]

An examination of " 229, male, Formosan, Chinese locally resident " in Boko Island (Pescadores) leads to the conclusion that there is much infection with *Wuchereria bancrofti* on it and probably on the other islands of the archipelago and on the main island.

Signs of filariasis were found in 99 and microfilariae in 37 ; and of these last the English summary states that there was chylocele in 7, inflammation of the testis and epididymis in 13, distension of the spermatic cord in 9, varicose groin glands in 1 and no physical signs in 7, a slight average increase of sedimentation rate, a normal blood pressure, an average erythrocyte count of 4,456,000, haemoglobin index 72, average leucocyte count 7,376, eosinophilia in 26. The presence or absence of other parasites is not noted in the summary. *C. L.*

HU (Stephen M. K.). **Notes on the Filarial Infection of *Culex pipiens* var. *pallens* Coq. in Relation to the Microfilarial Density of the Blood.**—*Lingnan Sci. Jl.* 1937. July 22. Vol. 16. No. 3. pp. 409–413.

The experiment consisted in feeding *Culex pipiens pallens* on two persons, one having many the other few *Mf. bancrofti* in the blood, and noting the numbers present in these insects on the fifteenth day.

Arranging the series in order of decreasing numbers of microfilariae in 20 cc. of blood at the hour of feeding on 3 different days, these numbers were 285, 176, 103, 25, 17 and 7. The percentages of mosquitoes which failed to become infective were respectively 12·5, 0, 40, 42·9, 56·4 and 77·7 ; of those which showed 1 to 9 larvae, the percentages were 45, 44·9, 55, 57·1 (1 to 4 larvae), 43·6 (1 to 4 larvae) and 22·3 ; of those showing 10 to 14 larvae, 7·5, 6·9, 5, 0, 0, 0. Only the mosquitoes fed on the blood containing 285 and 176 microfilariae to 20 cc. of blood showed greater numbers, the greatest being 80 in one mosquito for the first and 77 in another for the second series. Again, of 89 mosquitoes fed on the heavy filarial case, 85·5 per cent. became infected, 55·2 per cent. harbouring 5 larvae or more, while of 71 fed on the light case 40·8 per cent. became infected and 1·4 per cent. harboured 5 to 9 larvae. *C. L.*

ABE (Shinichi). **Investigations on the Biological Behaviour of the Mature Larvae of *Wuchereria bancrofti* developed in the Mosquito.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1937. Sept. Vol. 36. No. 9 (390). [In Japanese pp. 2083–2102. [37 refs.] English summary pp. 2102–2103.]

" A study was made of the biological behaviours of the mature larvae of *Wuchereria bancrofti* that had undergone full development in the formosan breed of *Culex quinquefasciatus* (C. fatigans). The method adopted followed closely that used by Wakeshima (1933) in his studies on tropism of the mature larvae of *Ancylostomidae*. A number of interesting results were obtained which are summarised below.

" The life of the mature larvae was comparatively long when left at generally low temperatures and in a closed place ; in other environments its

life was shorter. It lived longest, 37–58 hours, when placed in normal saline, but was extremely sensitive to drying and usually died in 1–2 minutes under such conditions. Its viability in different media including various fruit juices" are given in a table. "*Thigmotropism* was not exhibited by this larva. At low temperatures *negative phototropism* was well marked, but when left at a temperature of 37–40°C. for one to one and a half hours, an opposite attitude was taken, and *positive phototropism* was demonstrated. There was no evidence of marked *thermotropism*. *Hydrotropism* could be demonstrated." [It is not made clear how a tropism to water can be tested in an animal already living in a watery fluid.] "*Chemotropism* for human blood and canine tissue fluid was not easily shown and was often overlooked. For oxygen and human bile there was definitely no evidence of *chemotropism*." *C. L.*

Joyeux (Ch.) & Sautet (J.). Contribution à l'étude de la culture des microfilaires. [**The Culture of Microfilariae.**]—*C. R. Soc. Biol.* 1937. Vol. 126. No. 26. pp. 361–362.

Microfilaria immitis grows in length in favourable artificial media.

The authors first note the different lengths given for these microfilaria by different workers, and point out that these differences are probably due to changes caused in preparation of microscope slides.

Survival for an average of 12 days took place in a mixture of the serum of a dog parasitized with *Dirofilaria immitis* and its total blood haemolyzed with distilled water. During the first 6 days there was an increase in the maximum length of embryos, measured without being fixed, from 280μ to 442μ, though when these latter were fixed in formol the maximum at six days was 377μ, and when seen in a thick drop 395μ. The growth had nearly reached its maximum in 3 or 4 days. There is no increase in breadth and no differentiation of organs. The laboratory temperature, or one of 4° to 9°C., seemed to make no difference to growth; and the lower temperature, seeing that it does not favour bacterial growth, was a real advantage. The use of the serum of a pregnant mare was of no advantage; and Row's medium unheated, and horse serum, were less successful. [Is not, then, the absence of such large forms in circulating blood presumptive evidence of the rapid destruction of microfilariae by the host's body?] *C. L.*

Montestruc (E.) & Bertrand (Ch.). Note sur l'étiologie et le traitement de la lymphangite tropicale. [**Cause and Treatment of Tropical Lymphangitis.**]—*Bull. Soc. Path. Exot.* 1937. Oct. 13. Vol. 30. No. 8. pp. 695–698.

Two cases of lymphangitis are described, both seemingly at Albert-Clarac.

One ended in suppuration at the apex of Scarpa's triangle on the right side, the abscess yielding both *Mf. bancrofti* and streptococci; the man had also acute funiculitis. The second had monthly attacks of lymphangitis in upper and lower limbs and breast. Apparently neither had elephantiasis, and no mention is made of microfilariae in their blood. It is thought that benefit was got from antistreptococcic vaccine in one, but not from antistreptococcic serum in the other. In the second, Rubiazol and Septazine were used in treatment.

C. L.

Gorter (A. J.). De operatieve behandeling van elephantiasis der onderste extremiteiten. [**Operative Treatment of Elephantiasis of the Lower Extremity.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1937. May 18. Vol. 77. No. 20. pp. 1236–1242. With 4 figs. on 2 plates.

The object of treatment must be to remove superfluous tissue along with excessive fluid and to ensure the restoration of lymph flow. In general enlargements of the lower extremities, constrictions of the swelling are found at the popliteal space and at the ankle. The surface of the skin is apt to be fissured and ulcerated. Preliminary treatment is absolutely essential. The limb is raised and the surface lesions are treated. This will take at least 10 days. Skin grafting, and excision of an ulcer may be necessary. The results of this treatment are usually remarkable. All this time the patient must be strictly confined to bed. Operation is performed in one stage only by the removal of elliptical portions of skin from the buttock fold down to the ankle. Two ellipses are required because of the narrowing of the general enlargement at the popliteal space, one above and one below. Careful measurements are to be made on the normal limb in order to judge how much to cut away, or rather how much to leave behind for the fashioning of a new limb. Obviously, any normal skin remaining will be spared for this purpose. The operation requires general narcosis and a rubber tourniquet is applied as high up the limb as possible. Undercutting of the skin may be required and this can be done with safety on both sides to the extent of 10 cm. Severe shock has not been found to occur as the result of the operation. The after-treatment is just as important as the preliminary treatment. First and foremost the limb must again be elevated, but bandaging of the limb is not in the first place desirable in case of hindrance to the circulation. Movements of the foot should be early encouraged, and, after a few days, some movement at the knee may be begun. No fixation of skin to muscles has been observed after operation. Stitches may be removed on the 9th day and, if no complication has occurred, the patient may be allowed up on the 14th day. He must now wear a supporting elastic bandage to the whole limb. On retiring to bed the limb must again be elevated, which may be done with the help of a sufficiently high cushion.

The results have been gratifying. No sign of oedema of muscles appears and a satisfactory lymph flow appears to become established. Patients have been observed for as long as 2½ and 5 years and their satisfactory condition has been maintained. *W. F. Harvey.*

Trewn (Harbans Singh). **Guinea-Worm.**—*Indian Med. Gaz.* 1937. Oct. Vol. 72. No. 10. pp. 606–609.

A paper written on an experience of 526 guineaworms removed during 3 years.

An editorial note points out that while it does not contain anything particularly original, the paper does show how the infection may be dealt with in an ordinarily equipped hospital. Points of more general interest are the appearance of a guineaworm in a convict of 15 years' standing; the presence of 56 worms in one person at the same time; a seasonal incidence; the importance of the "step well" in the causation of the infection, with instances where infection ceased

when a covered well took the place of these tanks ; the immunity of some to infection although they are using the same sources of water as do others who get a yearly infection ; the injection of 1 in 1,000 corrosive sublimate solution into the worm itself, with a dressing over the sore of the same solution, is highly thought of. *C. L.*

KOFOID (Charles A.), WILLIAMS (Owen L.) & VEALE (N. C.). *Thelazia californiensis,* **a Nematode Eye Worm of Dog and Man, with a Review of the Thelazias of Domestic Animals.**—*Univ. California Public. Zool.* 1937. Vol. 41. No. 17. pp. 225–233. [30 refs.]

A redescription of *Thelazia californiensis* based on specimens from dogs. In them measurements are on the whole larger than from worms parasitizing man. Transmission experiments with cockroaches, or by feeding the larvae to dogs or instilling larvae into their conjunctival sacs were negative. The adults' rapid movements make their removal from the conjunctiva a difficult matter. *C. L.*

HABERT (M.). Fièvre jaune et tétrachlorure de carbone. [**Yellow Fever and Carbon Tetrachloride.**]—*Bull. Soc. Path. Exot.* 1937. July 7. Vol. 30. No. 7. pp. 598–601.

The record of two patients who, after taking 3 cc. of carbon tetrachloride, both showed symptoms closely simulating yellow fever, in one case even developing "black vomit."

A third (fatal) case is discussed in which the histological examination of the liver resulted in a diagnosis of "toxic infection hepatitis" of yellow fever type. It was found that this patient became ill immediately after taking a dose of carbon tetrachloride.

E. Hindle.

MEDICAL AND SANITARY REPORTS.

SUDAN (1936).

The Sudan is bounded on the north by Egypt, east by the Red Sea, Eritrea and Abyssinia, south by the Uganda Protectorate and Belgian Congo, west by French Equatorial Africa. Its western and northern frontiers meet in the Libyan desert. The greatest length north to south is approximately 1,300 miles and from east to west 1,200 miles. Its total area is about 1,008,100 sq. miles.

Vital Statistics.—For previous observations under this heading the reader is referred to this *Bulletin*, 1936, Supp., pp. 90*–92*, and 1937, Supp., p. 100*–101*. Population figures are to be regarded as only rough estimates and as such are of very limited value in the determination of birth and death rates: the distribution of these estimated populations reads as follows:—

Province.	Approximate Population	Province	Approximate Population
Blue Nile	809,599	Kordofan	1,222,729
Darfur	751,528	Northern	508,030
Equatorial ...	1,051,059	Upper Nile ...	536,647
Kassala	409,355	White Nile ...	388,347
Khartoum	267,183	Total ...	5,944,477

At present no machinery exists whereby accurate vital statistics can be assembled, but the Report presents data for Khartoum and Blue Nile Provinces, Berber, Blue Nile, Dongola and Wadi Halfa Districts, births, stillbirths, and deaths with distinction as to sex, and deaths in age groups. Summarizing these facts we have:—

Nationality	Births	Stillbirths	Deaths
Europeans	26	1	29
Sudanese	18,525	489	10,506
Egyptians and Syrians	267	7	57
Others	351	3	439
Totals	19,169	500	11,031

The following facts are also given for *non-Europeans*:—

Area	Births	Birth Rate	Still-births	Still-birth Rate	Deaths	Death Rate	Infant Deaths	I.M.R.
Khartoum Prov....	4,223	15·8	118	27·9	2,650	9·9	265	62·7
Berber Dist. ...	3,837	20·3	116	30·2	1,925	10·2	205	53·4
Dongola Dist. ...	5,024	26·2	156	31·0	2,550	13·2	232	46·1
Blue Nile Dist. ...	4,806	11·6	81	16·8	3,253	7·8	164	34·1
Wadi Halfa Dist....	1,253	18·9	28	22·3	624	9·4	73	58·2

[It is presumed the stillbirth rates are calculated per 1,000 live births. With reference to birth and death rates see this *Bulletin*, 1937, Supp., p. 101*.]

Government Officials of British nationality numbered 820; two were invalided and two died during the year. Other Government Officials employed were, *Sudanese* 3,836 with 4 invalidings and 14 deaths; *Egyptians* 537, 2 invalidings, 4 deaths; *Syrians* 49, no invalidings or deaths.

The average annual strength of the *Sudan Defence Force* was 4,440. During the year 3,669 N.C.O's and men were admitted to hospitals suffering from various forms of disease. *Malaria* headed the list with 977 cases—most of these occurring among troops operating in unhealthy areas along the eastern boundary. *Wounds and injuries* follow next in order with 708 cases, attributable to extensive movements of troops, and increasing mechanization of equipment. *Venereal diseases* were responsible for 508 cases, of which 278 were due to *gonorrhoea*, 188 to *syphilis* and 40 to *soft chancre*.

Maternity and Child Welfare Work.—Valuable work, highly appreciated by all classes of the population, continues to be carried out at established clinics (see this *Bulletin*, 1937, Supp., p. 101*). It is noted that of the 9,085 attendances recorded at clinics in Khartoum Province, 2,926 related to new cases. The returns of the Civil and C.M.S. hospitals, the Medical Training School, and trained midwives in Omdurman (from the latter source data for the first half of the year only) show that 1,109 women were treated for diseases of *pregnancy*, *childbirth*, *etc.*, and 11 died, and of 1,018 births recorded, 977 were live births. Hospital returns also show that 646 gynaecological and 446 labour cases were dealt with, 642 of the former and 425 of the latter relating to non-European women; among the 425 native labour cases 22 deaths were registered.

At the *School of Midwifery*, Omdurman, 25 pupil midwives completed their training and passed the qualifying examination, while 5 trained midwives attended revision courses. Of the 269 midwives trained at this *School* during the past 16 years, 224 are still in practice in various parts of the Sudan; their inspection is carried out regularly by the Inspectress and Matron of the School. So successful has the work proved that there is an increasing demand on the part of Sudanese women to be delivered in hospital or to be attended by a trained midwife. The stage has been reached when the work of the School is to be supplemented by the establishment of a subsidiary centre at Juba in the Southern Sudan.

School Hygiene.—It was found possible to extend the work of the School Medical Service in most provinces of the Northern Sudan; more attention was also paid to village schools especially with a view to the earlier treatment of trachoma and other eye conditions. During the year 21,041 children were examined; *trachoma* remains the major cause of disability in the North and *malaria* in the South. No case of *pulmonary tuberculosis* was discovered. A year ago in these pages it was noted that the percentages of children affected by *trachoma* varied between wide limits not only as between Province and Province but even between Districts in the same Province. These variations continue; the lowest recorded percentage is of 1·8 for a school in Khartoum Province, and the highest 91·3 for one in White Nile Province. In Khartoum Province out of 2,814 children examined, 1,055 were suffering from trachoma and among 1,250 pupils there were

233 cases of defective vision. Routine treatment of trachoma has proved most effective. Incidence of the disease among pupils of the Gordon Memorial College declined further to 21·7 per cent. (see this *Bulletin*, 1937, Supp., p. 102*). As regards malaria incidence among school-children, spleen rates—which are given for various Districts in the nine Provinces—range from 0·7 per cent. in Wadi Halfa in the Northern Province to 47·2 per cent. at Fung in the Blue Nile Province. It is pointed out that while in the Northern Sudan the figures provide fairly accurate indices of malaria endemicity, in the Southern Provinces, where schools are few, the data may prove misleading.

Public Health, Sanitation, etc.—The epidemic of *cerebrospinal meningitis* which continued from 1935 and spread to every Province in the Northern and Western Sudan adversely affected the state of the public health during the year under review. Moreover, in the Northern Sudan, the rains were heavy, late, and badly spaced and these together with the irregular fall of the Nile and formation of residual pools, provided conditions favourable to mosquito breeding with the result that malaria incidence was considerably higher. Though these developments heavily taxed the resources of the public health staff, the *Sanitary Services* were nevertheless extended and consolidated in towns and in most Provinces. In Dongola good progress was made in the provision of properly constructed *pit latrines* in private houses, while in the smaller towns, with the appointment of qualified sanitary overseers, health organizations were established where hitherto sanitation was perfunctory or absent.

Though no new purification plants or piped *water supplies* were installed during the year, projected schemes for Wadi Halfa, Malakal, and Torit are being considered. The routine examination of established supplies continued to give satisfactory results (see this *Bulletin*, 1937, Supp., p. 102*).

The question of *housing improvement* received special attention, for the epidemic of cerebrospinal meningitis again emphasized the importance of overcrowding as the main factor in the spread of the disease. In the Northern Sudan steady progress is reported in the clearing of insanitary and overcrowded areas and the construction of an improved type of dwelling. A committee was appointed to consider the best types of native houses from the economic and hygienic point of view.

The six *Sudanese Sanitary Officers* are proving a valuable addition to the public health service; it is intended to post at least one such officer to each province where British staff is not available. Sanitary Overseers (see above) undergo a course of instruction in Khartoum; during the year 36 candidates qualified and were posted to various towns and districts.

Training, Medical, etc.—To the Kitchener School of Medicine 10 new students were admitted, and there are now 24 medical and 6 sanitary students on the registers. Six out of seven medical students were successful at the Final Examination and will be posted to the larger hospitals for one year on probation. In the course of training for Assistant Medical Officers—who in outlying districts where no sanitary staff are available are responsible for public health work—instruction is given in the principles of hygiene and sanitation.

Port Health, Quarantine, etc.—Ships entering Port Sudan numbered 1,604. None was quarantined but 3 persons from ships were isolated during the year. Quarantine restrictions for cholera were enforced at

times during the year against ships arriving from Siam and Ceylon, for smallpox against vessels from Bombay and Karachi, and for plague against ships from Karachi. The *Suakin Quarantine Station* dealt with 3,404 pilgrims; all were vaccinated and received one inoculation against cholera; 151 were admitted to hospital and 7 died. At Wadi Halfa 1,152 Egyptian labourers passed through the quarantine; none were repatriated as unfit, though 66 were found to be infected with bilharzia and were treated.

All *aircraft* arriving at, or departing from frontier aerodromes are inspected and disinsectized; during the year 2,371 machines were dealt with at five aerodromes. All mosquitoes captured are identified by the Medical Entomologist and a record kept of their probable port of origin.

Hospitals, Dispensaries, etc.—With the completion of the new Omdurman Hospital it is believed that hospital facilities—providing approximately one bed per 1,000 population—will be as adequate as can be supervised and maintained efficiently. Future aims will be directed towards the provision of X-ray sets, better laboratory equipment, etc., and to raising the standards of efficiency of the subordinate staff. There are now 337 dispensaries established in various parts of the Sudan; no appreciable increase in their number is envisaged in the near future.

There appear to be 6 *Mission Hospitals*, of which 4 are maintained by the Church Missionary Society, one by the Sudan United Mission, and one by the American Mission. Of *Mission Dispensaries* there are 12, *viz.*, Sudan United Mission 6, Italian Mission 3, American Mission 2, and Church Missionary Society 1. Work accomplished at Government and Mission treatment centres during the year may be set out as follows:—

Item	In-patients	Deaths	Out-patients
40 *Government* Hospitals, and 337 *Government* Dispensaries	96,081*	2,308*	6,500,441
6 *Mission* Hospitals	1,990	?	113,454
12 *Mission* Dispensaries ...	—	—	50,194†

* 95,620 of the in-patients and 2,294 of the deaths relate to non-Europeans.
† Data are supplied for two Dispensaries only.

Courses of training are organized for Assistant Medical Officers, Dispensers, Hospital Orderlies, Hospital Nurses, and other categories of medical and sanitary personnel (see also *Training, Medical, etc.*, above).

The notes which follow briefly summarize the more important items of 1936 morbidity experience commented upon in the Report under review:—

Malaria remains the most important public health problem with which the Sudan authorities have to deal, for though the disastrous epidemics of past experience no longer sweep the country, much disability and loss of life are still attributable to the disease. Mention has already been made of the factors responsible for considerably increased incidence experienced during the year. In certain parts of the Northern Province the disease assumed almost epidemic proportions, but it is observed that in the Southern half of the Province

where sanitary services have recently been reorganized and strengthened, there was no epidemic malaria despite adverse climatic conditions.

According to official returns, at Government institutions 189,713 cases of the disease were dealt with, and of this total 10,310 of the patients received in-patient hospital treatment, and 74 died. Of *blackwater fever* 38 cases were reported with 14 deaths, the racial distribution being Arab Sudanese 24 cases, 11 deaths; Negroid Sudanese, one non-fatal case; British 3 cases, 1 death; other races 10 cases, 2 deaths.

The distribution of spleen rates among school-children is briefly referred to in the Section *School Hygiene* above. It remains to add that *subtertian* malaria appears to be the prevailing infection. In the Blue Nile Province blood films examined for the presence of malaria parasites contained 1,790 *P. falciparum*, 194 *P. vivax*, and 65 *P. malariae*, while at the Stack Medical Research Laboratories in 1,006 blood films examined, the corresponding findings were 133, 41, and 2 respectively.

Anti-malarial work is being extended, but outside the towns little can be done in this direction owing to the prohibitive cost of effective measures. In these circumstances protection of the individual both in urban and rural areas is aimed at as the principal measure of defence (see also under *Scientific* below).

The epidemic of *cerebrospinal meningitis* (see *Public Health* above and this *Bulletin*, 1936, Supp., p. 96* and 1937, p. 104*) continued to rage with increased severity. During the year under review 13,440 cases and 8,906 deaths were recorded, or four times the number of cases and deaths recorded in the preceding year; morbidity and mortality due to this disease were greater than any experienced during the past seven years. All provinces were affected—Darfur Province had 8,833 cases and 6,158 deaths, Kordofan Province 2,293 cases and 1,386 deaths, while at the other end of the scale were Port Sudan and Suakin 3 cases 2 deaths, and the Equatorial Province one fatal case only.

Despite every effort to localize the epidemic, the disease spread rapidly during the first six months of the year, finally dying away with the beginning of the rains. The only effective prophylactic measure under field conditions was the evacuation of villages to specially constructed shelters in the open country—where possible a separate shelter was constructed for each person (see this *Bulletin*, 1936, Supp., p. 96* and 1937, Supp., p. 104*). No curative measures that are possible on a large scale have yet been evolved—anti-meningococcal serum was used in a number of cases but results were not encouraging.

At the Stack Medical Research Laboratories local strains of meningococci were isolated and examined with results that were confusing. It is stated that "In view of this antigenic overlapping it seems distinctly unlikely that the group sera at present issued from the Standard Laboratory are likely to afford any help in an antigenic classification of strains in the Sudan or act as a guide to specific serotherapy," and again "there has been no clear evidence that the polyvalent serum used in a number of cases in 1936 had any specific influence on the infection." [In the 1935 Report mention was made of experiments being conducted by Dr. N. L. Corkill with Vitamin A extract as a prophylactic; results were said to justify further experiment (see this *Bulletin*, 1937, Supp., pp. 104*–105*),

but no mention of these researches appears in the Report under review.]

Smallpox introduced by Abyssinian refugees into the southern districts of the Blue Nile Province, gave rise to 501 reported cases and 132 deaths. An outbreak of chickenpox in the area at the same time may have made differential diagnosis difficult in many cases. A small outbreak in a hill district of Kassala Province caused 31 non-fatal cases ; a mild form of the disease made its appearance in two districts in the Equatorial Province resulting in 43 non-fatal cases, and there were also two cases among pilgrims in the Suakim Quarantine Camp, one of which proved fatal. During the year 82,272 primary and 10,677 re-vaccinations were performed.

Of *diphtheria*, 63 cases were reported, 34 of these occurring in the Northern Province where the disease has persisted for some years among a sparse and scattered population south of Wadi Halfa. All the cases received in-patient hospital treatment and 12 died. Among 739 throat swabs examined at the Stack Laboratories 46 were positive with *C. diphtheriae*. Twenty-two non-fatal cases of *relapsing fever* occurred in the Singa District of the Blue Nile Province, and a mild form of *influenza* appeared in epidemic form during the winter in the Northern Sudan. *Undulant fever* was responsible for 58 cases and 4 deaths, 15 of the cases occurring in the Blue Nile Province, 14 in the Equatorial and 12 in Kassala Province. At the Laboratory 48 out of 646 samples of serum agglutinated *Br. melitensis*.

The incidence of *rabies* remains high. Hospital Returns show that 64 persons (two were Europeans) received treatment as in-patients and 8 died, while 373 persons received anti-rabic treatment during the year. In one case treatment was commenced 4 days after the bite, a full course of injections was given, yet hydrophobia developed on the 85th and the patient died the next day. At the Stack Laboratories among 115 brains received for examination 42 were positive for *Negri bodies*, 34 being dogs, 5 donkeys, 1 cat, 1 sheep, and 1 rabbit (inoculated from a human case).

Kala-azar is mildly endemic in an extensive belt of country adjoining the Abyssinian and Eritrean frontiers. Incidence of the disease remains fairly constant. During the year 214 cases and 28 deaths were reported, the main centres of distribution being 111 cases in Blue Nile Province, 52 in the Equatorial Province and 21 in Kassala Province. Of the total cases recorded 106 occurred among Arab Sudanese and 91 among Negroid Sudanese. All cases received in-patient hospital treatment.

Enteric fever gave rise to 135 cases with 17 deaths ; 133 of the cases were hospital in-patients and 17 died (6 European cases, 1 death). As usual the majority of the cases were due to *Bact. typhosum* infections. Sanitary improvements in the town of Dongola have proved successful in bringing about a decrease in incidence of the disease, and in Khartoum Province the number of notifications was fewer than in any year since 1932. At the Stack Laboratories Widal tests were applied to 646 samples of serum and 90 reacted positively with *Bact. typhosum* ; diagnosis by blood cultures in 434 samples examined gave 59 *Bact. typhosum*, 4 *Bact. paratyphosum A*, and 1 *Bact. paratyphosum B*, while in 711 specimens examined *Bact. typhosum* was isolated in 45 cases. A certain amount of work was carried out on the Vi antigen of *Bact. typhosum* and the results published in the *Journal of Hygiene*, Vol. 36, p. 368. The inagglutinable strain isolated from a child (see

this *Bulletin*, 1937, Supp., p. 106*), was proved to be a typical V, with a high virulence for rats and gerbils.

The incidence of *dysentery* is said to be declining, and with further sanitary improvements it is hoped this decline will continue. During the year among 2,564 hospital cases 2,393 were amoebic and 171 bacillary infections; 55 deaths were ascribed to amoebic and 6 to bacillary dysentery. Among the hospital cases were 17 European patients, of which 14 were suffering from the amoebic form of the disease. At the Stack Laboratories where 1,390 faecal specimens were examined, the types of organisms isolated were *Bact. dysenteriae* (Flexner) 24, Shiga 19, Schmitz 9, and Sonne 2.

During the year 150 new cases of *sleeping sickness* were reported; all occurred in two areas in the Equatorial Province close to the frontier. Easy intercommunication with infected areas across the frontier and the local topography which is ideal for tsetse-fly breeding add to the difficulties of dealing with the problem in the endemic areas. All possible precautionary measures are taken; the pass system for travellers to and from Uganda functions satisfactorily (see this *Bulletin*, 1937, Supp., p. 106*). The Government Entomologist reports the receipt of a specimen of *Glossina morsitans* from an area in the Nuba Mountains, whence no "fly" has been recorded for many years.

Tuberculosis.—Of the 868 cases admitted to hospitals 519 were of the *pulmonary* form of the disease; out of 141 deaths recorded 117 were ascribed to *phthisis*. Of the total cases recorded 764 occurred in the Northern and 104 in the Southern Sudan; only 7 cases occurred among Europeans, 6 of these being due to pulmonary tuberculosis.

Eye diseases.—Dr. A. R. McKelvie contributes his usual *Ophthalmic Report*. According to Hospital Returns 268,015 in- and out-patients were treated for *trachoma* during the year under review; at the River Hospital 565 in-patients were treated for this affection, and there were also 23,318 attendances recorded among out-patient cases, the corresponding figures at the Omdurman Hospital being 90 and 32,367 respectively (see also *School Hygiene* above).

Helminthic diseases.—Hospital Returns provide the following data relating to these infections:—

	In-patients	In-patients and Out-patients
Schistosomiasis ...	1,146	10,858
Dracontiasis	647	3,716
Ankylostomiasis ...	572	2,947

As regards *schistosomiasis* it is observed that during the past 12 years, measures have been directed towards the prevention of infection of the canals and indigenous population in the irrigated area of the Gezira, a district exposed to the constant risk of infection from the thousands of immigrants who enter, a large percentage of them suffering from the disease. To date these measures have proved successful. The annual surveys in parts of the Northern and Blue Nile Provinces gave the following results:—

Area	Number Examined	Number Infected	Percentage
Northern Province (2 Districts) ...	37,334	1,268	3·4
Wadi Halfa District	12,437	1,439	12·9
Blue Nile Province	28,087	27	0·09

Dracontiasis continues as a cause of considerable disability in the Southern Sudan and in the Nuba Mountains. In the former area special wells are being constructed to reduce the incidence, but in the Nuba Mountains the situation is more difficult owing to the existence of numerous infected pools in the hills. It is noted that of 3,716 cases treated in all areas during the year 3,225 were in the Equatorial Province. *Ankylostomiasis* is said to occur only in a few isolated areas in the Northern Sudan, and that measures taken to prevent the introduction of infection have reduced incidence to negligible proportions. In the Equatorial Province the disease is widely distributed on the Western side of the White Nile but is rarely met with on the east of that river.

Leprosy is believed to be well under control throughout the Sudan where it is estimated there are 10,495 lepers with 7,933 of them in the Equatorial Province alone. At the end of the year there were 2,550 lepers in camps or settlements and 889 under observation or treatment. The system of home isolation at present carried out in the Northern Sudan is said to work well, while in the Southern Sudan where the incidence is higher, settlements have been established near dispensaries and have functioned satisfactorily. It is only in the southern districts of the Equatorial Province that leprosy is a menace, and there both the large and small settlements function as satisfactorily as can be expected.

Extracts are again given from the Report of Dr. WOODMAN, Senior Medical Inspector, Li Rangu (where one of the big leper settlements is established) in the Yambio District. Among other matters he states that there are 3,648 known lepers in the Yambio sub-district and approximately 850 in the Meridi and Iba sub-districts, and that the conclusions reached and described in the preceding report still hold good (see this *Bulletin* 1937, Supp., p. 107*). From among relapsed cases, and those having persistently declined in spite of previous treatment, selected groups have been given experimental courses of treatment with various dyes, so far without evidence of permanent benefit from their use.

Of *venereal diseases* it is stated that little change in their incidence can be reported. The investigations of the Obstetric Surgeon continue and show that the incidence of *syphilis* among pregnant women though high is not a common cause of abortion. Among 40 cases of abortion, 38 were Kahn tested and only 5 or 13 per cent. reacted positively. [It is regretted that in the preceding issue of this *Supplement* it was stated in error that 94 per cent. of tested cases reacted positively in 1935; actually the proportion was 9·4 per cent.]. During the year Port Sudan was notified internationally as a port at which sailors could obtain free V.D. treatment in accordance with the terms of the Brussels Convention. The incidence of yaws is said to have been reduced to negligible proportions except in the extreme south.

The Report under review which states that 77,571 cases of *syphilis* and *yaws* were treated during the year also contains the following :—

Disease	Hospital In-patients		Sudan Defence Force N.C.O'S. and Men.
	Europeans	Non-Europeans	
Syphilis	—	11,157	188
Gonorrhoea	1	2,285	278
Soft Sore	2	495	42
Yaws	—	944	2

Other diseases include mention of 89 cases of *scurvy* with 2 deaths, 7 of *beriberi*, and 3 of *pellagra*. Dr. H. A. CROUCH reports that there is reason to believe that in many areas the population exist in a state of subnutrition. *Tumours* were responsible for 758 cases of which 192 were malignant and the cause of 42 deaths. At the Stack Laboratories among 140 pathological specimens received 104 were defined as malignant tumours. Any attempt to analyse details with distinction as to age and sex would be misleading—in most cases age is not given and fewer women than men submit to operation for neoplasms. *Hydatid disease*, which appears to be confined to the Taposan tribe round Kapoeta, caused 10 cases, while of *acute rheumatism* 288 cases and 5 deaths were reported, with the greatest incidence in the Northern, Kordofan, Blue Nile, Khartoum, and Kassala Provinces.

Scientific.—Under various headings in the preceding notes mention has been made of the various specimens received for examination at the *Stack Medical Research Laboratories*, and of the findings recorded. It remains to say that during the year under review examinations of all kinds totalled 18,041 with among them a considerable increase in the number of routine Kahn tests (exclusive of those carried out at the Port Sudan Hospital Laboratory), *viz.*, 11,490 as compared with 9,320 in 1935. Tallqvist's method of haemoglobin estimation has been abandoned, the Sahli-Hellige Haemoglobinometer adopted and this apparatus issued to six of the large hospitals ; the technique of the use of the latter instrument is now taught as a standard method to all assistants under training. The *yellow fever* investigations continue (see this *Bulletin* 1937, Supp., p. 109*), the work including examination of liver sections from fatal cases of pyrexia of obscure origin, mouse protection tests with sera collected from the natives of the Eliri district of the Nuba Mountains (results indicating a wide-spread infection of the virus of yellow fever in that area during the last 20 years), and similar tests with sera obtained from monkeys and cows. These investigations will be extended to include the sera of other domestic and wild animals. Other work included the preparation of vaccines, experiments carried out with strains of seed lymph received from Lagos and from the Government Lymph Institute, Colindale. These experiments and the results obtained are described in some detail.

The *Government Entomologist* contributes a separate report of the activities of his department. This included surveys of insects of medical importance, the collection and identification of insects from aeroplanes, experimental work concerned with determining the efficacy of stocking pools with *Gambusia affinis* for the control of mosquitoes. Results, which are to be embodied in a paper for

publication, suggest that this species of fish is not effective for the purpose in artificial pools in urban areas. A detailed account of a survey of anophelines in the Gezira Irrigated area is supplied; *A. gambiae* was found to greatly outnumber other species and is the only proved vector of malaria in the area. The Report concludes with reference to the use of larvicides, methods of trapping adult mosquitoes, and the occurrence of mosquitoes other than anophelines.

P. Granville Edge.

NORTHERN RHODESIA (1936).

Northern Rhodesia lies north of the Zambezi River with Tanganyika Territory and the Belgian Congo to the north, Nyasaland and Portuguese East Africa on the east, Southern Rhodesia and South-West Africa on the south and Portuguese West Africa on the west. The area of the Territory is estimated at about 287,950 sq. miles and divided for administrative purposes into nine Provinces.

Vital Statistics.—Though estimates of the native population were made for each of the years 1930–34 in the Report under review, it is stated "There is probably justification for saying that the native population numbers something over a million and a quarter; beyond that I would not venture to go and as no figure is obtainable for total births or total deaths that could be regarded as even approximately reliable, no attempt has been made to calculate rates." (See also this *Bulletin*, 1937, Supp., p. 79*.)

Knowledge of the *European population* is also conjectural. An estimate of 14,000 is stated to be "little more than a guess and does not justify the calculation of birth and death rates."

On the assumption that *European births* are correctly and fully registered, there were recorded 313 and of *European deaths* 78: *malaria, blackwater fever,* and *accidents* were among the principal causes of death. There were six *European infant deaths.*

European Officials resident numbered 611 with an average number resident of 536; the corresponding figures for *Native Officials* were 2,550 and 2,376 respectively. There were no invalidings or deaths among European Officials, but 25 Native Officials were invalided and 13 died during the year under review.

Maternity and Child Welfare Work.—At European Hospitals 185 women were treated as in-patients for *diseases of the puerperal state,* 142 being cases of normal labour; at Native Hospitals the corresponding figures were 107 and 56 respectively. The addition of a maternity section separated structurally from the main building is a necessity at the Lusaka Hospital.

The four *Welfare Clinics* were maintained (see this *Bulletin*, 1937, Supp., p. 79*). The only records of work presented in the Report relate to two of these Clinics, *viz.*:—

Clinic	Europeans		Natives		
	Patients	Attendances	Men	Women and Children	Attendances
Lusaka ...	179	354	2,423	4,335	30,979
Ndola ...	142	4,771	1,347	4,991	26,173

Reference is made to the large volume of successful welfare work carried out by the three copper mining companies ; a nursing sister and subordinate native staffs are employed by each of these concerns for work among the dependants of mines native employees.

School Hygiene.—Government Medical Officers inspected all European Schools and scholars twice during the year ; a good deal of evidence of malnutrition was noted together with numerous cases of enlarged tonsils. Organizations for arranging seaside holidays for children are established in Ndola and Lusaka, and have operated with great success. Dental inspections of school-children are made twice yearly, but the complaint recurs that in too many cases parents fail to have remedied the defects discovered (see this *Bulletin*, 1937, Supp., p. 80*). In all schools both native and European lessons in hygiene are given and the subject is an item in the syllabuses of teachers in training.

Public Health, Sanitation, etc.—Dr. J. F. C. Haslam observes that financial considerations again prevented any increase of staff " either by way of restoration of officers retrenched in 1933 or otherwise," and that in consequence the pressure of work has so taxed the energies and resources of medical officers as to give rise to no little concern. Provision made for the medical care of the native population is inadequate ; of the 12 medical officers' stations established in an area larger than France, as 10 are sited primarily in European interests, it is obvious that considerable aggregations of natives must be beyond the reach of medical aid.

Though available statistical information regarding the general health of the population is negligible as to quantity and unreliable as to quality, it is believed that no notable improvement or deterioration in the public health occurred during the year under review. Apart from a staff of medical officers too occupied with clinical duties to be able to give much time to preventive work, the Department had three Health Inspectors (one on leave during the year) whose primary duties were concerned with the organization and implementation of preventive measures. Having regard to the very considerable shortage of staff and money, but little could be accomplished despite the evident determination on the part of all concerned in their struggles to " make a shilling do a pound's work." In the chief centres of *European population* it is claimed that fair standards were maintained with respect to *disposal of excreta and rubbish*, *water* and *food supplies*, and the prevention of the grosser forms of nuisance. In the previous Annual Report it was stated that the water supply of Lusaka was adequate in quantity ; Dr. Haslam observes that the storage capacity of the tanks is, however, deficient.

During 1936 organized recruiting of *labour* for employment in the Rand mines increased, and a considerable stream of natives leaves voluntarily for employment outside Northern Rhodesia. The conditions under which native labour is employed at the three large copper mines and at Broken Hill mines are excellent ; employees of the Zambesi Saw Mills, Limited, are less adequately dealt with, but conditions are described as fair and in process of improvement. The medical care of employees in agriculture is inadequate (see this *Bulletin*, 1937, Supp., p. 80*). The *housing* of agricultural labourers hardly anywhere attains the standards legally prescribed, and on many farms is described as " frankly bad." It is also observed that the

accommodation provided for servants of Government officers in Livingstone is unsatisfactory in many cases.

Under the heading of *Food in Relation to Health and Disease*, observations remain as previously described (see this *Bulletin*, 1937, Supp., p. 81*). It is noted that a committee has been appointed to report on nutrition in the Territory.

Training of Sanitary Personnel.—The first training school for African Medical Staff in Northern Rhodesia was opened on the 1st October, 1936, and 24 pupils able to read, write, and speak some English were enlisted mostly from Mission Schools. As soon as it becomes practicable to extend the scope of the present teaching, which is confined to the training of hospital assistants, the training of Africans as *sanitary inspectors* will be undertaken.

During the year under review *Ordinances and Regulations* enacted in the interests of *Public Health* had reference to such matters as *building, drainage*, and *latrines, sale of bakery products, ice, aerated waters, etc.*

Recommendations submitted to Government have reference to the the staffing of the Medical Department, medical arrangements at Broken Hill, and reorganization of the present system for the distribution of medical stores and equipment.

Port Health Work remains as previously described (see this *Bulletin* 1937, Supp., p. 81*).

Hospitals, Dispensaries, etc.—No additional hospitals were built, and no existing hospitals were replaced by new buildings (see this *Bulletin*, 1937, Supp., p. 81*), though minor improvements were carried out at several institutions. At Lusaka the new hospital needs a separate building for maternity cases, and new premises for isolation purposes. The native hospital at Abercorn remains housed in a building condemned as a gaol [the Report says " condemned as a goal "] seven years ago, while the native hospitals at Fort Jameson and Lusaka are dark, unsuitable, and inconvenient, and stand in need of replacement ; application has been made to the Colonial Development Committee for financial assistance for the improvement of medical services. Government maintained 18 *rural dispensaries* staffed by native orderlies ; some of them can accommodate a few in-patients (see also this *Bulletin*, 1937, Supp., p. 81*).

The *Mining Companies* continue to maintain admirably staffed and equipped European and native hospitals, while various *Missions*, subsidized by Government to the extent of £3,050, do valuable medical work in outlying districts.

The work carried out at the various hospital centres may be set out as follows :—

Institution	In-patients			Out-patients
	Admitted	Treated	Deaths	
Government Hospitals—				
7 European	1,652	1,691	23	?
12 Native	10,009	10,700	402	52,151
Dispensaries	—	1,534	—	24,160
Mining Companies	6,571	?	95	?
Missions	No details supplied.			

It is observed that though hospital figures show a steady increase in the volume of work, the latter is not indicative of increased morbidity, but of increased confidence in, and use of facilities available.

Malaria continues to be the chief cause of sickness among Europeans; during the year 486 admissions to European hospitals were recorded, and 493 cases were treated, with 2 deaths. All were subtertian infections. To hospitals for natives, there were 1,067 admissions, 1,088 cases treated, and 25 malaria deaths registered; here also all were subtertian infections. Of *blackwater fever* 14 cases among Europeans with 2 deaths and 2 non-fatal native cases were recorded. It is stated that European cases of blackwater fever occur mainly among members of the poor Dutch farming community, where standards of living and nutrition are very low.

Malaria was very prevalent in the new capital of Lusaka during the early months of the year. Steps were taken to drain the only permanent anopheles breeding-place dangerously near the new township. Prison labour was employed with success. It is believed that an appreciable reduction in Lusaka malaria rate may be expected to follow completion of this work. As regards general anti-malarial works it is noted that the approved estimate for such services amounted only to £915.

Among the *notifications of infectious diseases* received were 22 European cases and 4 deaths due to *blackwater fever* (see above). Also there were 9 European and 24 native non-fatal cases of *typhoid fever*; Hospital Returns quote 9 European cases of *typhoid*, 3 of *paratyphoid undefined*, and 6 native cases of *typhoid*. Notified cases of *dysentery* among Europeans numbered 24, of which 14 were amoebic, 3 bacillary, and 7 undefined; all were non-fatal. Among natives there were 194 cases with 3 deaths, distributed as to 38 amoebic, 17 bacillary, and 139 undefined.

Smallpox.—No case of variola major was reported, but a small outbreak of variola minor occurred in the Mazabuka District where 96 cases were recorded with no mortality; 10,712 vaccinations were performed. No case of *plague* was recorded (see this *Bulletin*, 1937, Supp., p. 82*). *Cerebrospinal meningitis* gave rise to 15 native cases with 8 deaths, 8 of the cases receiving in-patient hospital treatment with 7 deaths.

Notified cases of *relapsing fever* are said to have totalled 186 (see this *Bulletin*, 1937, Supp., p. 82*). All were native cases and one death only was ascribed to this cause. It is noted that 21 cases were reported from Kasama, 77 from Mongu, and 90 from Fort Jameson, making a total of 188.

Influenza was less prevalent and less virulent in type than in the preceding year. Four cases among Europeans and 698 among natives were notified, with 78 deaths among the latter. Though several small epidemics of *measles* were reported, fewer cases were reported and mortality was less severe among children. There were 126 non-fatal cases among Europeans, and 224 among natives with 16 deaths. Of *scarlet fever* 9 non-fatal European cases were notified, 30 cases of *whooping cough* among Europeans and 94 among natives, 8 European cases of *diphtheria* (one death) and 2 native cases.

Of *trypanosomiasis* the Report records 28 notified cases among Europeans, and none among natives though five deaths of natives were ascribed to the disease (see this *Bulletin*, 1937, Supp., p. 83*).

Dr. Haslam states that evidence is accumulating to show that *tuberculosis* is more prevalent than has been supposed. During the year under review 8 Europeans and 83 native cases of the disease (all forms) were notified; of these totals *pulmonary tuberculosis* was responsible for 2 of the European cases with 1 death, and for 75 of the native cases with 16 deaths. *Pneumonia* continues to menace the health of the native population; at Government native hospitals where 351 cases of the disease were treated with 100 deaths, 119 of the cases and 36 of the deaths were due to *lobar-pneumonia*, while unclassified pneumonias were responsible for 188 cases and 47 deaths.

With regard to *helminthic diseases* it is stated that increasing information shows these diseases to be more prevalent than was realized (see this *Bulletin*, 1937, Supp., p. 83*). Hookworm infection is widespread but not severe; Medical Officers report the finding of ova by routine stool examinations in cases showing no symptoms of infection. *Schistosomiasis*, both urinary and intestinal, is common in some areas. Hospital Returns show 3 cases of *ankylostomiasis* among Europeans and 169 among natives, 11 natives treated for *S. haematobium* 86 for *S. mansoni* infections.

Reported outbreaks of *rabies* among jackals and dogs occur every year and give rise to anxiety and increasing expenditure upon vaccine for the protection of contacts. During the year under review 44 outbreaks were reported, 21 being experienced in Mazabuka alone.

Venereal Diseases.—Facilities for treatment remain as described in these pages a year ago. *Syphilis* continues to be as prevalent as ever in the Namwala District where there is no resident medical practitioner, either Government or Missionary. Medical Officers comment upon the rarity of stricture as a sequela of untreated or partially treated *gonorrhoea*. According to Hospital Returns, 4 Europeans received treatment for gonorrhoea; natives treated included 2,073 cases of *syphilis*, 242 of *gonococcal infections*, and 3 of *soft chancre*. There were also 294 natives treated for *yaws*.

Scientific.—Dr. Haslam repeats last year's recommendation for the early provision of a medical laboratory (see this *Bulletin*, 1937, Supp., p. 84*). As matters stand only routine examinations of urine, blood, and stools, were possible during the year. Native microscopists stationed at the large hospitals continued to do useful work, and those attached to the Lusaka Native Hospital, under the supervision of Dr. Board, who is in charge of the newly established Native Medical Training School (see above), carried out 4,164 laboratory examinations during 1936.

Financial.—Expenditure on Medical Department services amounted to £65,091, a sum representing 7·5 per cent. of the total revenue of the Colony during 1936. *P. Granville Edge.*

REVIEWS AND NOTICES.

STITT (E. R.) [M.D., Sc.D., LL.D., etc.], CLOUGH (Paul W.) [M.D., etc.] & CLOUGH (Mildred C.) [M.D.]. **Practical Bacteriology, Haematology and Animal Parasitology.** Ninth Edition.—pp. xiii + 961. With 208 figs. & 4 plates. 1938. London: H. K. Lewis & Co., Ltd. [30*s.*]. [Review appears also in the *Bulletin of Hygiene.*]

This well-known book, previously published under the direction of the senior author only, has again increased in size and one may truly say in usefulness.

The general arrangement follows broadly that employed in the previous edition but in detail the material has been eclectically selected and considerably rearranged.

Part I contains chapters on the general principles of bacteriology and on the systematic study and identification of bacteria. It also has a chapter on the filtrable viruses which is almost entirely new and an entirely new one on the fungi. Other useful sections are those dealing with the bacteriology of water and milk, with the principles and problems of immunity, and with serological methods.

Part II, which has been considerably expanded, is devoted to haematology, and in no part of the book has the revision been greater than in this section. Special attention has been paid to the technique of blood examinations, and methods which are regarded as useful and important are described in detail. In addition to all the routine examinations other less-often practised procedures, as for example sternal puncture or the production of Price-Jones curves, are described, and such matters as the medico-legal application of blood grouping in cases of disputed parentage are discussed. In the present edition a number of new illustrations appear, and in this section on haematology two coloured plates and two coloured drawings illustrating normal and pathological blood conditions have been introduced.

Part III of the book is concerned with animal parasitology and concisely summarizes an extraordinary amount of useful data.

Part IV deals with the pathological examinations of the various fluids and organs. It includes various functional tests with explanations of their underlying physiology, and there are chapters ranging from such matters as recent views on the function of the endocrine glands to detailed considerations of the principal food deficiencies.

The appendix contains a number of sections dealing with apparatus and stains, with media and material, and with the chief laboratory procedures useful in diagnosis.

The authors state that they have contrived to bear in mind the needs of those in tropical or remote fields, who do not have access to well-equipped libraries, and to all such workers the book can be warmly recommended. It will, however, have a much wider appeal for it represents a very able attempt to bring together in handy form, within obvious limitations, a vast amount of laboratory and field data, and to correlate with the clinical picture all those ancillary aids which are so necessary for the adequate solution of modern medical problems. *F. Murgatroyd.*

Bulletin of the Health Organisation. (League of Nations.) 1937. Dec. Vol. 6. No. 6. pp. 895–1153. **The Treatment of Malaria. Fourth General Report of the Malaria Commission.**

This report is concerned with the comparative values of quinine and of synthetic drugs in the prophylaxis and treatment of malaria. Special importance attaches to an authoritative report of this kind.

The Malaria Commission of the League of Nations has formulated certain guiding principles and has fully and clearly described the advantages and disadvantages of each method of treatment. The rôle of the Malaria Commission is primarily to keep Health Administrations informed of such advances in malariology as may be of service to the community, and to help them to distinguish what is proved from what is still doubtful. Where the truth is not plainly revealed the Commission endeavours to assess the value of measures or methods by arranging experiments according to a specific programme. This is what happened in the present instance. In 1935 a plan for testing methods of treatment and for experiments in mass drug prophylaxis in the field was elaborated. Countries showing very diverse epidemiological conditions were selected for the experiments. They were Algeria, Italy, the Federated Malay States, Rumania and the Union of Soviet Socialist Republics. Observations were carried out on a total of 12,288 persons. The five national reports, four of which have been published and noted in this *Bulletin*, form the main basis of this Fourth General Report of the Malaria Commission, but consideration has also been given to other relevant scientific contributions that have been published between 1933 and 1936. In the coordinated experiments the synthetic drugs were used in the manner suggested by the inventors of the drugs in question.

The Report consists of three parts :—An introduction in which the genesis of the inquiry and the manner in which it was carried out are described ; a critical study of the results of the inquiries ; and conclusions. Three appendices are attached. The first consists of the U.S.S.R. report. (The Health Section of the League proposes to republish this Fourth General Report of the Malaria Commission, with all relevant information, in the form of a special volume.) The second appendix is a review of the literature of the therapeutics and collective drug prophylaxis of malaria contributed by E. J. Pampana, the Secretary of the Commission, and the third contains the observations of certain members of the Malaria Commission, concerning the general report, which it was not possible to incorporate in the report itself. These observations, for the most part, do not express dissent from any of the fundamental findings of the Commission which, in all essentials, can be considered as unanimous.

It is not possible in a note of this kind to do more than direct attention to a few of the facts that emerge from these studies.

A daily dose of 0·50 gm. of quinine hydrochloride sometimes causes a temporary disappearance of trophozoites of *P. vivax* and of *P. malariae*, but a daily dose of 1·0 gm., for from five to seven days, is often necessary to cause their disappearance (on an average on the third day) and to remain absent till the first relapse after a varying interval of time. A daily dose of 1·30 gm., in some countries 2·0 gm., is necessary to produce similar results with *P. falciparum*. Quinine in the doses mentioned acts on the young forms of *P. vivax* and of *P. malariae* that are capable of producing gametocytes and also on fully

developed gametocytes. Its action on fully developed gametocytes of *P. falciparum* is very slight but it impedes the formation of pre-gametocytes; for this species quinine is, therefore, directly schizonticidal and indirectly gametocidal. On the acute clinical symptoms of primary benign tertian infections quinine has a definite action from the third day; its action is less reliable and less rapid in malignant tertian infections. The frequency of relapses after quinine treatment is influenced by individual factors and the strain of the parasite. It may be as high as fifty per cent. in primary cases of *vivax* and *malariae* infections that have been treated with the usual dose, 1 gm. daily. Quinine reduces splenomegaly if suitable treatment be given in each attack; this effect is but transitory if exposure to reinfection is frequent. If quinine treatment, in the doses mentioned, be limited to the strictly necessary number of days it has no adverse effect on the patient's general condition, nor does it appear to hinder the process of immunization.

Atebrin, in daily doses of 0·30 gm., has a slightly more rapid action on *P. vivax* and *P. malariae* trophozoites than has quinine in 1·0 gm. doses, and the absence of clinical symptoms after atebrin treatment lasts somewhat longer. On the trophozoites of some strains of *P. falciparum* atebrin acts more promptly than does quinine. It does not devitalize the gametocytes of *P. falciparum*, but its action on the gametocytes of *P. vivax* and *P. malariae* is perhaps slightly more marked than that of quinine. The action of atebrin on clinical symptoms of an acute attack is very marked; in some endemic regions this action is more energetic in *falciparum* than in *vivax* infections, but not in others. The action of atebrin on relapses is more effective than that of quinine. The spleen rate in communities treated with atebrin decreases somewhat more slowly than in communities treated with quinine but the effect is somewhat more lasting. The yellow discolouration of the skin caused by atebrin is a disadvantage, especially during prolonged prophylactic treatment.

Plasmoquine has little if any action on the trophozoites of *P. falciparum*, some slight action on those of *P. vivax*, and considerably more on those of *P. malariae*. Small doses associated with quinine or atebrin, however, sometimes appear to reinforce the action of these drugs on the trophozoites of both *P. vivax* and *P. falciparum*. Plasmoquine acts on the gametocytes of all three species but especially on those of *P. falciparum*. Doses of 0·02 gm. devitalize *falciparum* gametocytes and diminish their number. There is no advantage in using plasmoquine alone for the treatment of the clinical symptoms of an acute attack of any form of infection. In association with quinine or atebrin, or administered after one or other of these drugs, it is effective in preventing relapses of benign tertian and quartan and also apparently of malignant tertian fever. The small doses of plasmoquine now generally used, 0·02 gm., have no depressing effect on the general state of the patient. Its prolonged use may exert some influence on the neoformation of haemoglobin.

Published results contain no evidence that quinine combined with atebrin in treatment serves any useful purpose. Quinine combined with plasmoquine is less toxic than atebrin and plasmoquine. For the treatment of adult groups under observation there is no contra-indication to the simultaneous use of quinine and plasmoquine, which shortens the duration of treatment. It is indeed one of the most effective means of treating benign tertian and quartan malaria.

The association of atebrin with plasmoquine appears to aggravate the toxicity of each. Consecutive treatment with atebrin first (0·30 gm. daily for five to seven days) followed by plasmoquine (0·02 gm. daily for five days) diminishes substantially the number of relapses in malignant tertian and, more especially, in benign tertian and quartan infections.

In ordinary cases of *P. vivax* infections it is almost immaterial whether quinine or atebrin be used for the treatment of the attack.

The aims of mass treatment are to secure the largest number of complete cures (intensive treatment of patients) and to reduce to a minimum the risk of anopheline infection by indirect or direct gametocyte therapy. There are large malarial areas, especially in the tropics, where such mass treatment is impracticable. Here it is desirable to provide adequate and easily available treatment for the clinical manifestations of the disease. Little or no medical supervision may be possible. In such circumstances the cinchona alkaloids are the most suitable remedy.

"Mass drug prophylaxis has a twofold purpose: (1) to protect the population undergoing prophylactic treatment from the clinical manifestations of endemic malaria, in order that its working capacity and comparative standard of health may be safeguarded without injury to its premunization, even in areas in which it is exposed to repeated reinfection; (2) to reduce, in due course, the sources from which local mosquitoes may be infected."

"No prophylactic method, unless applied to disciplined communities under stringent supervision is capable as yet of attaining these two objects." Administered throughout the transmission season daily doses of 0·40 gm. of quinine, or bi-weekly doses of 0·20 gm. of atebrin give useful results. The daily dose of 0·05 gm. of atebrin is inadequate. Medical supervision is necessary if atebrin be used. The proportion of gametocyte carriers is commonly higher among children than among adults; the doses and form of administration of atebrin and plasmoquine to children is not finally settled. The eradication of malaria from an endemic locality by curative and prophylactic treatment alone is impossible with the drugs at present available, though much benefit may be conferred on the population concerned.

The administration of quinine preparations and, all the more, of synthetic drugs, by the parenteral route, should only be resorted to in special circumstances or cases. *Norman White.*

ERRATUM.

Vol. 35, No. 2, pp. 163–164, review of Bernard NOCHT's book "Malaria. A Handbook of Treatment, Parasitology and Prevention"; in the last line but one of p. 163 and the first line of p. 164, relating to quinine treatment, for "grams" read "grains".

Printed under the authority of HIS MAJESTY'S STATIONERY OFFICE
By The South Essex Recorders, Limited, High Road, Ilford.

(576) Wt. P11/202 1875 5/38 S.E.R. Ltd. Gp. 353.

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